X-Yne Click Polymerization

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**ABSTRACT:** Alkyne-based click polymerizations have been nurtured into a powerful synthetic technique for the synthesis of new polymers with advanced structures and versatile functionalities. Among them, the emerging thiol-yne, hydroxyl-yne and amino-yne click polymerizations have made remarkable progresses from reactions to applications. All three polymerizations avoid the usage of inherently dangerous monomer and are safer to operate than the classical azide-alkyne click polymerization, making them more prospective for widespread applications. To greatly promote the new alkyne-based click polymerizations beyond the azide-alkyne click polymerization, we propose a new concept of “X-yne click polymerization” to unify them. In this Perspective, we mainly give a brief account of the progression of X-yne click polymerization and discuss in detail the challenges and opportunities in this field.
1. Introduction

Development of new and efficient polymerization methodology is essential for polymeric material science. Among the established polymerizations, the click polymerization,\(^1\) stemmed from click chemistry and inherited all the superior features of it, such as high efficiency, mild reaction conditions, good regio- and/or stereoselectivity, atom economy, great functionality tolerance and orthogonality, has become a powerful tool for the preparation of polymers with novel structures and versatile functionalities.\(^2\) Additionally, the participant of alkyne monomers in the click polymerization may endow the resultant polymers with more properties such as electroactivity because of the unique unsaturated structures in their main-chains.

Azide-alkyne click polymerization (AACP) is the most classic and well-developed alkyne-based click polymerization, which can be classified roughly into three categories of Cu(I)-catalyzed, Ru(II)-catalyzed and metal-free ones according to the catalytic systems.\(^3,4\) Although the former two types have become powerful tools for the preparation of linear and hyperbranched 1,4-regioregular and 1,5-regioregular polytriazoles (PTAs),\(^5-7\) respectively, the metallic residues in resultant PTAs are difficult to be completely removed, which hinder their applications in optoelectronic and biological fields.\(^8,9\) The latter avoids the usage of transition-metal catalysts but to some extent at the expense of regioselectivity,\(^5,10\) and sophisticated monomer synthesis may also be required such as preparations of cyclooctyne derivatives.\(^11\) The connection of electron-withdrawing units such as carbonyl groups and perfluorophenyl moiety with the ethynyl and azide groups, respectively bestows the desired regioselectivity on the reaction.\(^1,12,13\) However, despite
the ongoing efforts of researchers on molecular design and catalyst optimization, the inherent explosive risk of azide groups is inevitable that limits large-scale preparation and further applications. Therefore, development of new click polymerizations without using azide groups is highly desired.

Over the last decade, we and others have developed a series of novel and efficient alkyne-based click polymerizations, including thiol-yne, hydroxyl-yne, and amino-yne click polymerizations.\textsuperscript{4,14} Compared with azides, these thiol, alcohol and amine-based monomers are safer during the usage and storage, and mostly easy to be synthesized or commercially available. Moreover, most of these polymerizations can proceed smoothly under mild reaction conditions, even spontaneously under ambient conditions.

Just like Staudinger put forward the concept of “macromolecule” and then opened the door of polymer science, the proposal of new concept is crucial to science development. To promote and unify these new efficient click polymerizations, we’d like to propose a new concept of “X-ynе click polymerization” in this Perspective, where “X” denotes the monomers that can react with alkynes by free-radical addition or nucleophilic addition, including thiols, alcohols and amines and others under mild reaction conditions. X-ynе click polymerization is a further refinement for click polymerization, and has the same click characteristics as AACP, but is safer than it because of no explosive azide monomers involved.

As an emerging and efficient polymerization methodology, X-ynе click polymerization has become systematic and can serve as a powerful tool for the synthesis of versatile polymeric materials. The current progresses are that new building blocks have been explored, new catalyst
systems have been invented, new reaction routes have been established, and new functional polymers have been created. It is worth noting that the X-yne click polymerization has received much attention from other scientific communities and been applied in many fields, including synthesis of polymer networks, hyperbranched polymers, sequence-controlled/defined polymers, unconventional elastomer materials and fluorescent polymers, surface modification and immobilization, bioconjugation and therapy as well as drug release, and so on.

In this Perspective, we briefly summarize the current progresses in X-yne click polymerization from reactions to applications and look forward to the future development. We also provide our opinions on how to tackle and grasp the challenges and opportunities that may lie ahead. It is hope that this Perspective will contribute to the further development of click polymerizations.

2. Progresses in X-Yne Click Polymerization

Herein, we mainly focus on the advances of thiol-yne, hydroxyl-yne and amino-yne click polymerizations. The influences of monomer design, catalyst selection, reaction condition optimization and other factors on polymerization results will be discussed in detail and the representative application examples will be elaborated. Moreover, the polymerization reactions which temporarily can’t meet the requirements of click polymerization owing to harsh reaction conditions or unstable polymer structures but hold the potential are also listed.

2.1. Thiol-yne click polymerization. Apart from AACP, thiol-yne click polymerization is another well-studied alkyne-based click polymerization. In general, thiol-yne click polymerization can be classified into four categories based on the catalytic systems, namely, photo/thermo-initiated, base-meditated, transition-metal catalyzed and spontaneous ones. Unlike its analogous
thiol-ene polymerization, thiol-yne click polymerization possesses the unique bis-addition feature that each ethynyl group is capable of consecutive reaction with two thiol groups. Thus, it is suitable for the preparation of highly cross-linked polymer networks with high sulfur content. For example, after Bowman et al. firstly used the photo-initiated thiol-yne click polymerization to synthesize highly cross-linked networks in 2009, Chiappone et al. utilized this method to produce new-type 3D printable materials (Figure 1A). The 3D objects with controllable components could be obtained by adjusting the relative ratios of ethynyl and thiol groups in printing formulations during the printing process, and the excess unreacted ethynyl groups could continue to react with azide-terminated squaraine dye by azide-alkyne click reaction so as to realize further functionalization of 3D objects.

Besides the polymer networks, Perrier et al. used an AB$_2$-type monomer bearing both thiol and ethynyl groups to prepare functional hyperbranched polymers by taking advantage of the bis-addition feature, where A and B represented the thiol group and the each π bond of ethynyl group, respectively (Scheme 1a). The AB$_2$-type monomer could be easily synthesized by sequential thiol-ene or thiol-halogen together with thiol-yne click reactions. When the ratio of thiol and π bonds of ethynyl group was 1:1, linear bis-addition polymers with side chains could be acquired (Scheme 1b).

Through the introduction of large hindrance substituent groups and rational condition control, mono-additive products can also be obtained solely. For instance, Voit et al. reported a series of linear and hyperbranched poly(vinyl sulfide)s (PVSs) constructed by thermo-initiated thiol-yne click polymerizations of aryl-substituted internal alkynes with dithiols (Scheme 1c). Despite
thiols were greatly excessive, all the PVSs were predominant or even only mono-addition units because of the large hindrance of aryl substituents. Moreover, the conjugation of the aromatic rings and the formed vinyl groups will also dis-activate the bis-addition of the later. The incorporation of high sulfur content, conjugated C=C bonds and aromatic groups endowed polymers with high refractive indices and moderate abbe numbers, rendering them prospective for optical applications. However, the broadened and overlapping NMR signals made it difficult to figure out the exact polymer structures.

**Scheme 1. Four Categories of Thiol-Yne Click Polymerization Based on Different Initiator/Catalyst Systems**
Later, Li et al. developed a catalyst-free thiol-yne click polymerization based on ester-activated internal alkynes and 4,4′-thiodibenzenethiol (Scheme 1d). The activation properties of ester groups increased the difference in the electrophilicity of the two ethynyl carbon atoms, thus improving the regioselectivity of polymerizations. In addition, the as-prepared polymers containing tetrphenylethylene (TPE) moiety exhibited aggregation-induced emission (AIE) characteristic.

Except for the thermo-initiated process, base-meditated thiol-yne click polymerization is another feasible tool for the preparation of PVSs. In 2010, Tang et al. reported an organobase-catalyzed thiol-yne click polymerization of ester-activated terminal alkynes and 4,4′-thiodibenzenethiol (Scheme 1e). With diphenylamine (DPA) as catalyst, sole anti-Markovnikov PVSs with high Z-stereoregularities (Z contents up to 81.4%) and high molecular weights (M_w up to 32 300) were successfully generated in high yields (up to 98.2%) under ambient conditions. Dove et al. also developed the organobase-meditated thiol-yne click polymerizations based on ester or amide-activated terminal alkynes and alkyl dithiols (Scheme 1f). By judicious choice of organobase catalyst and solvent polarity, the stereochemistry of the formed vinyl group could be precisely controlled so as to impact a lot on polymer properties, such as crystallization behaviours, mechanical and thermal properties. Thanks to the abundant alkyl chains in polymer skeletons and moderate crystallization, the resultant polymers could serve as thermally-processable elastomer-like materials with tuneable mechanical properties. What’s more, Dove et al. incorporated degradable succinate as co-monomer and prepared a new type of resorbable elastomer-like materials for bionic soft tissues regeneration (Figure 1B).
stoichiometry of succinate incorporation, the degradation rate of the materials could be tuned precisely while retaining control over the mechanical properties by maintaining the $E/Z$ ratios of the vinyl groups. After implanted in a subcutaneous rat model, the variant containing 100% succinate incorporation was capable of degrading *in vivo* over a period of four months and were gradually replaced by mature and developing tissues with limited inflammation, which showed huge potential for biomaterials applications.

In addition to the organobase, inorganic base could also catalyze this polymerization coupled with higher $Z$-stereoselectivities. Qin and Tang et al. found that, in the presence of $K_3PO_4$, aromatic diynes and aromatic dithiols could be faciley polymerized in $N$-methyl-2-pyrrolidinone (NMP) at 100 °C, producing 100% $Z$-stereoregular PVSs in high yields (Scheme 1g) after 24 h. While 100% $E$-stereoregular adducts could be obtained by the polymerization of aromatic alkynes and dithiols with the catalysis of rhodium complexes under ambient conditions (Scheme 1h). In addition, Markovnikov-selective thiolation of alkynes was realized by the promotion of Rh$^1$(NHC)-based catalyst, and the vinylidene content was up to 80% (Scheme 1i). The adjacent vinylidene groups and sulfur atoms in products could be selectively hydrogenated and oxidized, respectively, offering the possibility of preparing functional materials. However, the Rh residue was hard to be removed completely that may adversely affect the optical properties of the polymers.

All the works mentioned above needed the help of UV light, heat, base or transition-metal catalyst, which complicated the experimental operations so as to limit their further applications to some extent. In 2014, Qin and Tang et al. successfully established a spontaneous thiol-yne click polymerization of aromatic alkynes and dithiols for the preparation of functional PVSs with linear
and hyperbranched structures (Scheme 1j). Simply mixing the monomers in equivalent molar ratio in THF at 30 °C could readily produce soluble and regioregular PVSs with high molecular weights ($M_w$ up to 85 200) in excellent yields (up to 97%) after as short as 2 h. The spontaneity and ease of operation of this polymerization made it a powerful tool for preparation of versatile materials. For instance, unlike conventional two-step polycondensation, Zhang et al. creatively synthesized the functional polyimides (PIs) with good optical properties and robust mechanical properties by spontaneous thiol-yne click polymerization (Figure 1C). The resultant PIs showed good tensile strengths as high as 114.9 MPa, high glass transition temperatures and thermal decomposition temperatures (up to 238 °C and 381 °C, respectively). Notably, one of the prepared polymer films, PI BPADA-TBT, demonstrated a comparable or even preferable refractive index and much lower birefringence than most of the previously reported PIs. This film possesses a refractive index exceeding 1.70 at 633 nm and transmittance above 81% at 450 nm, making it a potential candidate in advanced optical applications. Recently, Chen and Tang et al. proposed a new strategy for the preparation of sulfur-containing polymeric photosensitizers (PSs) by this spontaneous thiol-yne click polymerization (Figure 1D). The introduction of sulfur atom induced a “heavy atom effect” so as to enhance the intersystem crossing (ISC) process of PSs, thereby further promoting the generation of reactive oxygen species (ROS). More importantly, this effect could be significantly amplified by polymerization. The introduction of AIE unit of tetraphenylpyrazine (TPP) also benefited the ISC by suppressing the non-radiative decay in the aggregate state. Moreover, the D-π-A structure consisting of weak electron donor of sulfur atom, TPP electron acceptor and vinyl π bridge, endowed the PSs with two-photon excited
photosensitization. The excellent two-photon excited properties of PSs combined with the high ROSs generation efficiency enabled them to perform well in the *in vitro* two-photon-excited photodynamic therapy towards cancer cells, and have great potential in the treatment of deep-tissue diseases.

![Figure 1](image)

**Figure 1.** (A) Chemical structures of the formulation used for 3D printing, together with the images of the 3D printed objects under bright field and fluorescence field, respectively. (B) Stereo-controlled synthesis of the resorbable elastomers, and subcutaneous *in vivo* degradation of poly(L-lactic acid) (PLLA) and samples with different stoichiometries of succinate incorporation and different cis% over 4 months. (C) Synthetic route to highly refractive polyimides. (D) Synthetic strategy for polymeric two-photon photosensitizers and schematic illustration of two-photon excited photoablation towards cancer cells.
2.2 Hydroxyl-yne click polymerization. Although oxygen and sulfur atoms belong to the same main group in the periodic table of elements, alcohols possess weaker nucleophilicity and lower reaction activity than thiols, which requires extra catalyst (usually an organic base) to activate the hydroxyl group. Thus, the reports on the polymerization of hydroxyl monomers and alkynes are also relatively scarce. In 2017, Qin and Tang et al. reported a superbase t-BuP₄ catalyzed hydroxyl-yne click polymerization of aromatic diynes and diols (Scheme 2a), from which soluble and thermo-stable anti-Markovnikov additive products with high molecular weights (\(M_n\) up to 40 600) were produced in high yields (up to 99%). The resultant poly(vinyl ether)s containing TPE moiety showed unique aggregation-enhanced emission (AEE) characteristic and their aggregates could be used as fluorescence probes to detect explosives with a superamplification quenching effect. In addition, the acid-responsiveness of vinyl ether bond made the polymers degradable under acidic conditions, and thus they are capable of being used as drug carriers. In addition, Qin and Tang et al. also successfully established a polymerization of internal alkynes of bromoalkynes and phenols, which was meditated by inorganic base of Cs₂CO₃. Thanks to their containing bromovinyl groups, the resultant polymers could be easily post-functionalized by thiophenols under ambient conditions (Scheme 2b). However, these two polymerizations both proceeded in high boiling point solvents at elevated temperatures that are unfavourable to their practical applications.

The introduction of electron-withdrawing group to directly connect with ethynyl groups will greatly make the reaction conditions more moderate. As shown in Scheme 2c, carbonyl-activated ethynyl (i.e. aroylacetylene) groups could be polymerized with diphenols in the presence of 4-dimethylaminopyridine (DMAP) at room temperature, affording sole anti-Markovnikov adducts
with 100% \(E\)-isomers in excellent yields (up to 99%). Density functional theory (DFT) calculations supported the proposed nucleophilic addition mechanism and unveiled the reason why only \(E\)-stereoregular products were favoured. Notably, this facile and efficient organobase catalysed hydroxyl-yne click reaction has been used for chemical modification of ethyl cellulose (EC) to prepare UV-blocking and fluorescent materials (Figure 2A). The residual hydroxyl groups of EC could be reacted with the ethynyl groups of 1-phenyl-2-propargyl-1-ketone (PPK) at room temperature. The degree of substitution mainly depended on the OH/PPK molar ratio, and could reach up to 82% when the OH/PPK molar ratio was 1:5. Simply mixing and stirring the THF solution of EC and PPK with DMAP for 5 min could reach more than 80% substitution, further proving the high efficiency of this reaction. The introduction of PPK moieties extended the thermal processing temperature range of ECPPKs compared with the pristine EC, and endowed ECPPKs with strong UV absorption performance and visible light excited fluorescence properties.

**Scheme 2. Examples of Established Hydroxyl-Yne Click Polymerizations**

Ester-activated alkyne is also an ideal candidate for hydroxyl-yne click polymerization. Compared with aroylacetylene groups, the alkyl or aryl propiolates can be easily synthesized by one-step esterification reaction of propiolic acid with diols or diphenols, which greatly facilitate
the development of propiolate-involved click polymerizations and their practical applications. Hence, Qin and Tang et al. subsequently succeeded in development of a novel hydroxyl-yne click polymerization based on bipropiolates and diols or diphenols monomers in the presence of an organobase bicyclo[2.2.2]-1,4-diazaoctane (DABCO) (Scheme 2d) under mild reaction conditions.\(^{35}\) The resultant polymers possessed different crystallization behaviours, semicrystalline or amorphous states, depending on the different flexibilities of monomers. Interestingly, the polymers composed of aliphatic chains only showed an \(E\)-isomeric configuration, while the participant of aryl alkyne or phenol monomers would impair the stereoselectivity of polymers. By taking the striking advantages of simple synthesis of propiolates and high efficiency of reaction, this click polymerization (reaction) has been applied in diverse areas. Different from the disordered structures of general polymers obtained by traditional polymerizations, sequence-defined polymers have definite structure compositions according to the feeding sequence.\(^{36-38}\) For example, as shown in Figure 2B, thanks to the great functionality tolerance of click chemistry, the DABCO-catalyzed hydroxyl-yne and \(N\)-heterocyclic carbene (NHC)-catalyzed thiol-ene click reactions were combined for the efficient protecting-group-free preparation of sequence-defined oligomers, the sequences of which could be encoded and decoded by tandem ESI-MS/MS spectrometry for high-density data storage.\(^{39,40}\) In particular, except for linear and homoarm star oligomers, the unprecedented miktoarm star oligomer was also constructed through the combination of the convergent and divergent synthetic strategies in an overall 68% yield, which could serve as a new-type topological digital macromolecule to achieve 2D information matrix encoding for information encryption. Apart from linear and star polymers, this DABCO-catalyzed hydroxyl-yne click
polymerization was also used to construct polymer networks and hyperbranched polymers. For example, Qin and Tang et al. successfully constructed a luminescent two-way shape memory polymer network by polymerization of dipropiolates and 4-arm poly(ε-caprolactone)s (PCLs) terminated with hydroxyl groups (Figure 2C). The as-prepared network PCL_{5800}-OH containing TPE moiety showed reversible shape transformation and remarkable blue emission, which could be fabricated into a micro robotic gripper. The gripper could grasp the screw pre-coated with a red-emissive AIE luminogen (AIEgen) in cool water (0 °C) and release it in warm water (39 °C) automatically and reversibly. The weight of the screw is 148 times higher than that of the gripper. Thanks to the introduction of AIE moiety, the grasp and release process could be clearly observed under UV light irradiation.

Besides in synthetic chemicals, hydroxyl groups are widely found in natural products, such as polysaccharides, amino acids and polyphenols. In view of the requirements of green chemistry, using natural products for polymer synthesis is the future development trend. Resveratrol (RSV) is a trifunctional polyphenol featured as excellent antioxidant and cardiovascular protective agent, as well as a synergistic drug with antitumor drug of doxorubicin (DOX) for the cancer treatment. Based on these, Meng et al. developed a pH-responsive and degradable hyperbranched polymer-based drug carrier via hydroxyl-yne click polymerization of trifunctional RSV and bifunctional propiolate. The drug carrier could co-assembly with hydrophobic DOX into nanoparticles in water and then break down under acidic tumor microenvironment due to the pH-sensitive vinyl-ether and vinyl-amino bonds, then releasing the covalently-bonded RSV and encapsulated-DOX for synergistic tumor chemotherapy (Figure 2D).
Figure 2. (A) Illustration of the modification of EC by hydroxyl-yne click reaction. (B) Synthetic strategy for the sequence-defined polymers by sequential hydroxyl-yne and thiol-ene click reactions and molecular structure of the miktoarm star oligomer. (C) Synthesis of the two-way shape memory polymer networks, together with schematic and photographic illustration of the reversible grasp-release process. (D) Synthesis process of the amphiphilic hyperbranched polymer RBP based on RSV and the preparation procedure of RBP@DOX nanoparticles.

2.3 Amino-yne click polymerization. Except for thiol-yne and hydroxyl-yne click polymerizations, amino-yne click polymerization has been developed rapidly and has become a promising tool for the preparation of nitrogen-containing polymers. In 2016, Qin and Tang et al. reported a Cu(I)-catalyzed polymerization of ester-activated internal alkynes and aromatic primary diamines (Scheme 3a). This polymerization could proceed smoothly in bulk with 100% atom
economy at 140 °C, producing sole anti-Markovnikov adducts with moderate molecular weights ($M_w$ up to 13 470) in high yields (up to 97%). Thus, they coined such type reaction as “amino-yne click polymerization”, which opens up a new pathway for the preparation of nitrogen-containing polymers. Qin and Tang et al. subsequently replaced the internal alkynes with terminal ones and found that the polymerization readily occurred when diynes and aliphatic secondary diamines were simply mixed in DCM at room temperature without any external catalyst (Scheme 3b). Through systematic optimization of the reaction conditions, solely anti-Markovnikov adducts with 100% $E$-isomer and high molecular weights ($M_w$ up to 64 400) were obtained in high yields (up to 99%). This spontaneous amino-yne click polymerization was also successfully used for the preparation of hyperbranched polymers. The spontaneity might result from both electronic effect and steric effect. On one hand, it has been demonstrated that electron-withdrawing groups can effective activate the ethynyl groups and increase their electrophilicity. And terminal alkynes may possess higher reactivity than internal ones because of the absent $\pi$-electron conjugation with benzene rings and reduced steric hindrance. On the other hand, the electron-donating inductive effect of alkyl substituents makes secondary amine monomers more nucleophilic than primary ones, and the site hindrance of the substituents makes it more inclined to generate trans-structures. Aliphatic primary amines could also be polymerized with alkynes under the optimized conditions but with a lower stereoselectivity ($Z/E = 60/40$) because the $Z$-isomers could be stabilized by the intramolecular hydrogen bonds. While aromatic amines could not react with alkynes probably owing to the $n-\pi$ conjugation between the lone pair electrons of amines with aromatic rings, which reduced the nucleophilicity of amines.
To further enhance the universality of amine monomers, carbonyl group with stronger electron-withdrawing ability was used to replace the ester one for the amino-yne click polymerization (Scheme 3c).\textsuperscript{48} Subsequent studies showed that different stereoregularities could be obtained by varying amine monomers. Similar to ester-activated alkynes, the polymerizations of carbonyl-activated alkynes with aliphatic secondary amines generated products with sole \(E\)-isomers, whereas the ones with only \(Z\)-isomers were obtained when secondary amines were used. Density functional theory (DFT) calculations unveiled that the \(Z\)-configuration product was favourable because of its lower Gibbs energy value with a small energy difference which was benefited from the formation of intramolecular hydrogen bonds. When the carbonyl group was changed to sulfonyl one, which has the strongest electron-withdrawing ability compared with carbonyl and ester groups, the resultant activated terminal diynes could be polymerized with all kinds of amines including aromatic and aliphatic primary and secondary ones, producing almost only \(E\)-isomers (up to 100\%) with high molecular weights \((M_w \text{ up to 160 000})\) in high yields (up to 99\%) under very mild conditions (Scheme 3d).\textsuperscript{49}

Notably, the formed enaminone moieties in this click polymerization was verified as a new-type dynamic bond and amine exchange occurred when another amine was added at elevated temperature. Taking advantage of the dynamic characteristic, the resultant polymers could be depolymerized upon the addition of primary amines. Similarly, the formed \(\beta\)-aminovinylsulfone moiety also possesses a dynamic feature, which endows polymers with degradability through amine exchange process. In particular, Lewis acid wasn’t needed in this process because of the greater electron-withdrawing activity of sulfonyl group.
Thanks to the simple operation, no need of catalyst and excellent polymerization results, the spontaneous amino-yne click polymerizations, especially the ester-activated alkynes involved ones, have been widely applied in the preparation of polymer networks, sequence-controlled polymers, and non-traditional intrinsic luminescent materials, and in biological field. As typical cross-linked polymer networks, hydrogels have unique swelling behaviours in water and have been served as a kind of biomaterials.\textsuperscript{50,51} Langer et al. successfully designed and prepared polyethylene glycol (PEG) based hydrogels via spontaneous click polymerization of PEG tetra-alkynoates and amines in aqueous media without using any initiator or catalyst (Figure 3A).\textsuperscript{52} The gelation kinetic and rheological properties could be regulated by adjusting the weight percentage of PEG tetra-alkynoates and amines relative to the total mass of water. Moreover, three-dimensional cell culture experiments indicated that these hydrogels had good cytocompatibility, making them promising in biomaterial applications. Similarly, Zhang et al. successfully prepared reversible metallacycle-crosslinked supramolecular polymer networks by combination of metal-coordination and spontaneous amino-yne click polymerization (Figure 3B).\textsuperscript{53} The introduction of rigid metallacyclic
structures not only offers the formed polymer network with good emission and self-healing properties, but also increases its adhesion strength and glass transition temperature, making it serve as a new type of supramolecular adhesive materials.

Meanwhile, the spontaneous amino-yne click polymerization was also applied in preparation of sequence-controlled polymers. Such polymers with ordered composition has become a hot research topic in recent years on account of their great potential in data storage and biological applications.\textsuperscript{54,55} However, existing synthetic approaches mostly require time-consuming reactions, and multi-pot processes or the use of DNA or RNA as templates,\textsuperscript{56} which severely limit their further development. From this point of view, click chemistry is well suitable for the preparation of sequence-controlled polymers owing to its high efficiency and simple purification procedures. Hong et al. combined the catalyst-free thiol-ene click reaction and amino-yne click reaction/polymerization to prepare sequence-controlled polymers in one pot under very mild conditions (Figure 3C).\textsuperscript{57} The sequence structures of polymers could be definitely and easily controlled by adjusting the feeding sequence according to the different reaction preference between thiol/amino and vinyl/alkynyl groups. This work provides an easy but efficient method for the preparation of functional polymers with controlled sequences. Moreover, thanks to its good compatibility with other reactions, amino-yne click polymerization has also been applied into multicomponent tandem polymerization (MCTP) together with ring-closing reaction for the preparation of poly(aminomaleimide)s (PAMs) with non-traditional intrinsic luminescent characteristic (Figure 3D).\textsuperscript{58} The resultant PAMs exhibited low cytotoxicity and were used as fluorescent bio-probes for bioimaging.
Besides the dynamic feature of the formed β-aminoacrylate by the click polymerization of ester-activated diynes and diamines, this bond is cleavable under external stimuli such as weak acid and reactive oxygen species, such as singlet oxygen \( (^1\text{O}_2) \).\textsuperscript{59–62} As shown in Figure 3E, the β-aminoacrylate moieties could be degraded into aldehyde and amine in a weak acidic environment, while \( N \)-formyl derivative and alcohol/phenol will be generated when singlet oxygen exists. Based on this unique cleavability, researchers have synthesized in succession a series of stimuli-responsive polymeric prodrugs by the spontaneous amino-yne click polymerization.\textsuperscript{59,61–64} For example, Ni et al. synthesized an ethynyl group-terminated amphiphilic copolymer via amino-yne click polymerization, whose terminal ethynyl groups then reacted with the amine groups of anticancer drug DOX through amino-yne click reaction to yield the drug-loading polymeric prodrug DOX-ena-PPEG-ena-DOX (Figure 3F).\textsuperscript{59} The prodrug was able to self-assemble into nanoparticles (NPs) in aqueous solution, and disassociate into amine and aldehyde derivatives under a weak acid environment (pH value below 6.5) on account of the acid-responsive cleavability of enamine bond, releasing the encapsulated DOX. \textit{In vitro} drug release behaviour study showed that 85% of original DOX could be released at pH 5.0. Cell test further demonstrated the prodrug NPs could be internalized into Hela cells through endocytosis and then release DOX owing to the acidic environment of cells, suggestive of the huge potential of this pH-responsive polymeric prodrug for cancer chemotherapy. Afterward, the single oxygen-responsive drug carriers were also reported. To overcome the cisplatin-resistance of tumours, Wu et al. designed a dual-responsive Pt(IV)/Ru(II) bimetallic polymer (PolyPt/Ru) constructed by amino-yne click polymerization,\textsuperscript{64} which could self-assemble into nanoparticles and accumulate in tumor site, then
be taken up by cisplatin-resistant cancer cells (Figure 3G). Under the irradiation of red light, the Ru(II) moieties could generate $^{1}$O$_2$ and escape from polymer skeleton through ligand substitution. The generated $^{1}$O$_2$ not only had the photodynamic therapy (PDT) effect for cancer cells but also further stimulated the cleavage of enamine bonds, inducing the disassociation of polymer chains. Meanwhile, the released Pt(IV) was reduced into the anticancer drug of cisplatin in the reductive microenvironments. Overall, the combination of the released Ru(II) anticancer agent and cisplatin as well as the generated $^{1}$O$_2$ realized a synergistic effect against cisplatin-resistant tumors.

Apart from being used as a building tool of drug carriers in biological applications, spontaneous amino-yne click polymerization itself could be served as an effective technique for bioimaging and therapy. As shown in Figure 3H, a lab-in-cell was successfully constructed by Qin and Tang et al.$^{65}$ In this work, the polymerization of carbonyl-activated diyne and an AIE-active TPE-containing diamine could proceed smoothly in cells by sequential feeding and incubation, producing poly($\beta$-aminoacrylate) with $M_w$ of 7 300. Thanks to the AIE feature of TPE moiety, the resultant polymers showed bright green fluorescence in cells, thus enabling a “turn-on” cell imaging. Meanwhile, in-situ killing was realized by destroying the structures of actin and tubulin of cells, which couldn’t be achieved by polymers pre-prepared outside the cell. This intracellular polymerization expands the biological application of click polymerization and holds great potential in bioimaging and therapy applications.
Figure 3. (A) Illustration of the preparation of β-(aminoacrylate) hydrogels. (B) Construction of the metallacycle-crosslinked polymer networks. (C) Synthetic strategy for the sequence-controlled polymers via the combination of thiol-ene click reaction and amino-yne click reaction/polymerization in one pot. (D) Synthesis of the non-traditional intrinsic luminescent PAMs, fluorescent images of PAMs in solution state and aggregate state, together with the merged confocal colocalization images of HeLa cells stained with PAMs. (E) Breakage of enamine bond
in the presence of weak acid or $\text{O}_2$. (F) Chemical structure of DOX-ena-PPEG-ena-DOX and schematic illustration of self-assembly, endocytosis and acid-responsive drug release processes. (G) Chemical structure of the amphiphilic triblock copolymer PolyPt/Ru and its disassociation process under red light irradiation, and schematic illustration of self-assembly, extracellular and intracellular processes for anticancer therapy using PolyPt/Ru. (H) Schematic illustration of the lab-in-cell constructed by sequential incubation, and synthetic route to poly(β-aminoacrylate).

It is well known that most novel polymerizations derive from and depend heavily on the development of high-efficient organic reactions. However, since spontaneous amino-yne click polymerization based on ester-activated alkynes was reported in 2017, this polymerization in turn has facilitated a wide range of applications of its homologous chemical reaction, that is, amino-yne click reaction. It has the advantages of high efficiency, mild reaction conditions and good compatibility with other reactions just like amino-yne click polymerization, which makes it very suitable for post-functionalization of polymers.\textsuperscript{66-69} For example, Qin and Tang et al. realized the site-selective, multi-step functionalizations of CO$_2$-based hyperbranched poly(alkynoate)s (hb-PAs) with nearly 100% conversion in each step via amino-yne click reaction and three-component polymerization/reaction of CO$_2$, alkynes and alkyl dihalides (Figure 4A).\textsuperscript{68} Because these two reactions didn’t interference each other during the synthesis process, one-pot, multi-step tandem polymerization with successive feeding and simplified purification procedures were realized. By introducing the hydrophilic oligo(ethylene glycol) chains and DOX into the branched chains and/or periphery of polymers, hyperbranched polyprodrug amphiphiles with high drug loading
content (44.3 wt%) were generated, what’s more, 78% loaded DOX at a pH value of 5.0 in vitro could be released owing to the acid-responsive enamine bonds. This work provided a powerful strategy for the post-modification of hyperbranched polymers into versatile functional materials. In addition, amino-yne click reaction was also been utilized for preparing multicolor fluorescent N,N-dimethyl-substituted boron ketoiminates (NBKI) with dimethylamino group as electron-donating unit, benzine ring as π bridge and unsymmetric OBFühr as electron-accepting unit (Figure 4B). The D-π-A conjugated system endowed NBKI with efficient fluorescent emission in solution. NBKI with varied optical properties could be obtained by adjusting the substituent in N-position via amino-yne click reaction. Moreover, multicolor fluorescent initiators based on NBKI were further prepared and used to initiate atom transfer radical polymerization (ATRP) and reversible addition-fragmentation chain transfer polymerization (RAFT), then producing a series of fluorescent polymers.

Bioconjugation plays an important role in the development of biomedicine and material science.71 However, there are many problems in traditional biological coupling methods, such as metal residues, complicated pre-modification and limited reaction efficiency. In 2018, Tang et al. put forward a metal-free bioconjugation strategy which was achieved by click reactions of activated alkynes and abundant native groups in biomolecules, including amino, thiol, and hydroxyl groups (Figure 4C).72 Thanks to the high efficiency of spontaneous amino-yne click reaction, pre-functionalization of biotargets and use of metal catalyst aren’t required, which help largely to simplify the conjugation procedures but still maintain the normal activity of biomolecules. Thus, this strategy enabled the high-efficient modification and functionalization of
natural polysaccharide, biocompatible PEG, synthetic polymers, cell penetrating peptide and protein, fast whole-cell mapping, and even quick differentiation and staining of Gram-positive bacteria. This work not only provided a general platform for facile biocompatible labeling of biotargets, but also provided a common approach for efficient modification of both organic and inorganic materials, definitely exhibiting broad prospects in the fields of biology, chemistry, and material science. For example, Qin and Tang et al. successfully expanded this metal-free bioconjugation method to fabricate the activated ethynyl functionalized surfaces for rapid immobilization of native proteins and cells (Figure 4D).\textsuperscript{73} Biomolecules such as bovine serum albumin (BSA), human IgG and a peptide of C(RGDfK) could be covalently fixed on the surfaces within 30 min while remaining their biological activity. In addition, Tang et al. applied this aminoyne click reaction in functionalization of silk.\textsuperscript{74} Silk is an important natural biopolymer in textile industry and biological applications, which is mainly composed of animal proteins and has abundant residue amino groups that are capable of reacting with activated alkynes.\textsuperscript{75} By chemically conjugated with activated alkynes bearing different AIEgens, fluorescent silks with full-color emission and high stability were facilely prepared. Compared with other fluorescent silks functionalized by physical absorption or non-covalent combination, AIEgen-silks constructed by bioconjugation showed the higher retention rates of fluorescence due to the stable covalent bonding. And white light-emitting (WLE) silk was also realized by simultaneous conjugation with blue-, green- and red-emissive AIEgens (Figure 4E). Moreover, the red emissive AIEgen-functionalized silks could be applied in long-term cell tracking and two-photon bioimaging. Furthermore, Tang et al. realized the accurate and long-term tracking of mitochondrial movement
in neurons by bioconjugation (Figure 4F). By elaborate structural design, TPAP-C5-yne with AIE feature could target at mitochondria and conjugate with amino groups on them. Then, under a confocal fluorescence microscope, an apparent change in the mitochondrial location was captured. Even after a week, the neurons stained by TPAP-C5-yne remained intact with bright fluorescence signal. This work provided more possibilities for neuroscience applications.
Figure 4. (A) Schematic illustration of post-modification of hyperbranched polymers by tandem multi-component polymerization/reaction together with amino-yne click reaction. (B) Synthetic routes of NBKI, CIE coordinate and fluorescence photos of NBKI derivates and related polymers. (C) Schematic illustration of the metal-free bioconjugation strategy based on activated alkynes and native groups in biology. (D) Schematic illustration of the fast and facile surface mobilization method. (E) Preparation of WLE silk and its fluorescence spectrum and CIE coordinate, together with fluorescence photos of flexible WLE fabrics fabricated from the AIEgen-silk fibers. (F) Graphic illustration of the bioconjugation of TPAP-C5-yne with mitochondria in neurons, confocal microscopy image of neurons stained with TPAP-C5-yne and recorded single mitochondrion trajectory in the 3D diagram.

2.4 Other potential X-yne click polymerizations. Expect for aforementioned three types of X-yne click polymerizations, there are actually other polymerizations being developed at the same time. However, some issues including product stability, reaction selectivity, complicated catalyst and additional energy input, limits the acceptance of these polymerizations as click polymerizations right now.

Organoboron compounds are widely used in organic transformations for their high reactivities and effective deborylation reactions. The hydroboration process is the most important method for the synthesis of boranes. As shown in Scheme 4a, hydroboration polymerization of diynes can proceed smoothly in THF at room temperature, producing regio- and stereoregular polymers in moderate yields. It seems to meet the requirements of click polymerization. However, decomposition experiments indicated that the polymers were unstable and underwent continuous
degradation under air and UV-irradiation, which may be attributed to the oxidation of vinylborane moieties to form the corresponding ketones.\textsuperscript{77} This inherent defect complicates the synthetic procedure and makes it hard to store the products for a long time, therefore influencing the further applications. While the air- and photo-stability are affected largely by the electronic effect and hindrance effect of substituents and can be improved by proper monomer design,\textsuperscript{78} such as replacing thexylborane with mesitylborane.\textsuperscript{79} If the stability problem could be settled out completely, this polymerization is potential to become a new type of click polymerization.

Similar to hydroboration process, hydrosilylation reaction has also been developed a lot. The operation simplicity of the hydrosilylation process, high tolerance towards various functional groups in the reagent structures, and the diversity of selectivities that can be tuned by appropriate catalysts, have rendered this transformation the preferred choice for synthesis of organosilicon compounds. For instance, Tang et al. utilized the polyhydrosilylation to prepare a series of \textit{E}-stereoregular poly(silylenevinylene)s with high molecular weights ($M_w$ up to 95 300) in moderate to high yields (up to 92\%) (Scheme 4b).\textsuperscript{80} Thanks to the high functionality tolerance, typical AIEgens, such as silole or TPE moieties, could be easily introduced into polymer backbones and endowed the resultant polymers with AIE feature. However, this polymerization depends heavily on the usage of expensive transition-metal catalyst, such as ruthenium, platinum, palladium and nickel catalyst,\textsuperscript{81–87} which makes it not “click” enough.

The development of new building blocks of polymerization is of great importance for the preparation of functional materials. Vinyl iodide groups are commonly enlisted for selective chemical transformations of small molecules, but are performed scarcely on polymer science due
to the limited methods for installing vinyl iodide groups into polymers. Sletten et al. put forward a novel iodo-yne polymerization assisted by sonication. In this work, perfluorodiiodide in which iodide atoms were activated by electron-withdrawing fluorine groups could react with alkynes under the initiation of Na$_2$S$_2$O$_4$, generating polymers with vinyl iodide functionality (Scheme 4c). Compared with other relative reports, this work could proceed in aqueous conditions using mild initiator, and realized the direct installation of vinyl iodide groups into polymer backbone, instead of the indirect post-modification of polymers that involved the pre-installation of activated functional groups such as vinylstannanes and then replacement by elemental iodine. However, this process required external energy input through ultrasound.

If the reaction conditions can be milder, avoiding the assistance of metal catalyst or sonication, hydrosilylation polymerization of alkynes and iodo-yne polymerization may be regarded as new types of X-yne click polymerizations.

**Scheme 4. Potential X-Yne Click Polymerizations**

3. Challenges and Opportunities

Although X-yne click polymerizations and their applications have made great progress in the past decade, there are still a large room for further improvement. Future challenges and opportunities lying ahead are urgent to be tackled and grasped.
3.1 Monomer scope expansion. Monomer is the cornerstone of a polymerization. Accompanying the expansion in monomer scope, the territory of click polymerization is also anticipated to be widened accordingly. Monomers involved in X-yne click polymerizations mainly consist of alkynes inactivated or activated by electron-withdrawing groups, and commercially available or easily synthesized nucleophilic ones. Previous experiments have shown that electron-withdrawing groups can efficiently enhance the electrophilicity and reactivity of alkynes compared with inactivated ones. Common electron-withdrawing groups include ester, carbonyl, sulfonyl, amide groups and halogen elements. It’s reasonable to speculate that other groups such as imide and sulfoxide may have the same effect. Despite these groups look a little similar, tiny differences in structures and reactivity may lead to huge distinctions in polymerization results and product properties. Furthermore, above activated alkynes will result in the partially conjugated polymers by the X-yne click polymerizations. The design and preparation of conjugated activated alkynes is another promising direction. In addition, compared with terminal alkynes, there are fewer reports on internal alkynes, which should be more concerned.

At present, polymeric raw materials mainly derive from the petrochemical industry. Actually, there are abundant functional groups, especially hydroxyl groups, in natural products such as monosaccharide (glucose), polysaccharide (chitosan), polyphenol (resveratrol) and amino acid (cysteine) (Scheme 5a). Using these natural products as monomers not only is in line with the concept of green chemistry, but also can lower production cost.89 There are several works involving natural monomers as building blocks for the construction of drug nanocarriers.26,36,60,61 However, these works focused more on the biology purpose, and natural monomer wasn’t the research priority.
Systematic studies of polymerization itself using these monomers are scarce. Solubility may be a big challenge in using natural monomers as building blocks. Because they are mostly water-soluble while alkynes are mostly dissolved in organic solvents, which may have a great impact on polymerization results. How to improve the compatibility through reasonable structural design and monomer choice is a problem that needs to be considered seriously. Moreover, other from traditional monomers, some natural monomers containing various groups with different reactivity simultaneously, such as amino acids, can be regarded as a new kind of unsymmetrical monomers. How to adjust the reaction conditions to make some groups reactive while others remain intact or make all groups reactive is challenging.

Carboxylic acid is also a promising candidate for X-yne click polymerization but works on it haven’t been reported yet. Resembling to hydroxyl group, carboxyl group can lose a proton under basic environment and generate the nucleophilic carboxyl anion, then attack the activated ethynyl groups. Similarly, amides and imides are less nucleophilic than amines owing to the existence of conjugated carbonyl groups unless they are converted into their more reactive anions when using base catalysts. Vilarrasa et al. found that a series of amides, imides and their derivatives could react with tosylacetylene to furnish enamine adducts with Z configuration in the presence of catalyst of Et₃N or NaH, while E-configuration products were generated when DMAP was used as catalyst (Scheme 5b). The adjustable and high stereo-selectivity together with excellent yields of this reaction indicated that amides, imides and their derivatives have great potential as new nucleophilic monomers for X-yne click polymerizations. In addition, amidine is also a promising candidate for the cyclic addition polymerization with ester-activated internal alkyne.
3.2 Polymerization development. Generally, most polymerization reactions are originated from organic reactions. The exploration of new organic reactions also promotes the development of polymerization. Current X-yne click polymerizations are primarily based on symmetric monomers that contain two or more identical functional groups. However, asymmetric monomers which possess two or more different reactive sites, such as amino acids mentioned earlier, have rarely been studied in polymerization. This kind of uncommon monomers accompanied by unique reaction mechanisms will help construct novel polymeric materials and thus induce new properties and applications.

The examples of two pseudo-three-component reactions based on difunctional reactants of imidazoline or oxime are shown in Scheme 6. In Scheme 6a, 1,2-disubstituted 2-imidazoline first underwent a Michael addition with an electron-deficient alkyne, thereby attached the vinylpropargylamine fragment at the N-position. Then, the second ethynyl group further attacked the α-position of nitrogen atom, leading to the disubstituted imidazoline.94 Notably, this reaction could proceed smoothly at room temperature in common aprotic solvents with moderate to high
yields. In Scheme 6b, oxime and two molecules of ester-activated alkyne occurred a diastereoselective (up to >99:1) annulation, generating polysubstituted β-lactams. The two reactions feature excellent substrate flexibility and benign functional group tolerance and the products are rich in nitrogen-containing heterocyclic rings, unsaturated bonds and carbonyl groups, which might bring some unique properties, such as nonconventional luminescence and self-assembly behaviors. In addition, the unsaturated bonds provide the possibility for further post-modification. If they are developed into polymerization reactions, the scope of X-yne click polymerization as well as polymer structures and properties will be greatly broadened. Theoretically, similar to thiol-yne click reaction, two hydroxyl groups can also be added to the same reaction site of triple bond to produce a bis-addition product (Scheme 6c). This reaction is interesting and promising for the preparation of metastable polymer networks or linear polymers with pendant groups.

Scheme 6. Organic Reactions Promising to Be Developed into X-Yne Click Polymerizations

and Schematic Illustration of Orthogonal Reaction
In addition to develop new polymerization reactions, the characteristics of the reactions themselves need to be thought about. One of the most attractive characteristics is the orthogonality of the reaction, which means that when several reactants (or functional groups) coexist, the click reaction can proceed independently while keeping others remaining intact (Scheme 6d). The combination of orthogonality and rapid reaction rate has made X-yne click polymerization be applied in the formation of interpenetrating dual network hydrogels\textsuperscript{101} and preparation of sequence-defined/controlled polymers\textsuperscript{40,57}, and so on. The orthogonal reactions can be achieved by proper monomer design, catalyst selection and reaction conditions adjustment according to the differences in reactive activity, catalyst system together with reaction conditions.

**3.3 Structural regulation.** The uniqueness of the X-yne click polymerization is that it will generate regio- and stereo-regular products. As shown in Scheme 7a, the mono-addition reactions can proceed through Markovnikov addition way to produce polymers with saturated mainchains and vinyl side groups, or undergo \textit{anti}-Markovnikov addition to furnish the unsaturated linear adducts with \textit{E} and/or \textit{Z} configurations. At present, polymerizations based on Markovnikov addition are much less explored than that of \textit{anti}-Markovnikov addition due to the limitation of catalyst system.

In general, the stereochemistry of vinyl groups is mainly affected by the catalyst choice, substrate design and solvent polarity. For example, configuration modulation on thiol-yne click polymerization has been successfully realized by adjusting the catalyst only. \textit{E}– and \textit{Z}-stereoregular and stereo-random PVSs were obtained under the catalysis of Rh(PPh\textsubscript{3})\textsubscript{3},\textsuperscript{26} K\textsubscript{3}PO\textsubscript{4},\textsuperscript{25} and in a catalyst-free way,\textsuperscript{28} respectively. The influence of substrates mainly includes both the electronic
and steric hindrance effects of substituent groups. For the systems involving intramolecular or/and intermolecular interactions, solvent polarity has a great impact on the Z/E configurations. Taking the catalyst-free model reaction of carbonyl-activated alkynes and amines as an example, when the reaction was carried out in a low polarity solvent such as DCM, sole Z-isomer was obtained using a primary amine (e.g., butylamine) because of the formation of intramolecular hydrogen bonds, while large steric hindrance of substituents on secondary amines (e.g., diethylamine) and absence of intramolecular hydrogen bonds resulted in the sole E-isomeric product. The Z/E-isomers ratio could readily be determined by $^1$H NMR spectra in CDCl$_3$. However, an intriguing conversion of E-isomer to Z-isomer was observed in other deuterated solvents, including acetone-$d_6$, toluene-$d_8$, MeCN-$d_3$, methanol-$d_4$, and DMSO-$d_6$. First, the $^1$H NMR spectra of E-isomer were recorded as quickly as possible after preparation. After 5 min, the E-isomer was predominated in all solvents. After 15 min, a significant shift from E toward Z-isomer was found in acetone-$d_6$, toluene-$d_8$, and MeCN-$d_3$, and eventually reaching an equilibrium of more than 84% Z-isomer in all cases, but exhibiting a 1:1 ratio in methanol-$d_4$ and a predominance of E-isomer (70%) in DMSO-$d_6$. This may be due to the competition between the intramolecular hydrogen bonds of products and the intermolecular interactions between the products and deuterated solvents. The high polar solvents such as MeOH and DMSO, disrupted the intramolecular hydrogen bonds required for stabilization of Z-configuration, leading to the dominance of E-isomers. Recently, we find that reaction concentration can also influence the E/Z isomerization, i.e., high concentration favors Z-isomer, while low concentration favors E-isomer. This might involve a competition between kinetic and thermodynamic control of the reaction process.
For the bis-addition reaction, to simplify the structure, we use mono-alkyne as an example to discuss. In this case, there are three possible linear saturated structures with side chains (Scheme 7b). If the mono-alkyne is replaced by diyne or multifunctional alkyne, corresponding polymer networks or hyperbranched polymers will be produced. Different structures may cause variation in the chain stacking of linear polymers and the pore size of the polymer networks.

It needs to be emphasized that we are not proposing a universal guideline for stereochemical control here. There are other examples that are not in full accordance with the trends mentioned above. All the factors act together, rather than independently, on the resultant configuration of products, the respective contribution of which remains unclear. Actually, a detailed understanding of the effects of catalyst system, substrate design and reaction solvent on the selectivity of X-yne click polymerization has not been fully investigated. Thus, more systematic study on the influence factors of regio-/stereo-control during the polymerization are needed urgently.

3.4 Functionality exploration. To make full use of the potential of X-yne click polymerization
for the practical applications, the exploration of its functionality is essential, which could be carried out based on the polymer structures. The examples are discussed below. The introduction of sulfur atoms effectively raised the refractive index of polymers, making thiol-yne click polymerization promising for optical applications.\textsuperscript{29} It’s found that both vinyl ether bond and enamine bond are labile under weak acidic conditions,\textsuperscript{44,59} and in addition, the enamine bond has an exceptional $^{1}\text{O}_2$-responsiveness.\textsuperscript{61} These unique characteristics make the corresponding polymers inherently degradable in the presence of weak acid or $^{1}\text{O}_2$ and has led to the widespread applications of hydroxyl/amino-yne click polymerizations in the construction of controlled release drug carriers. Notably, the enamine bonds connected with sulfonyl or carbonyl groups were successively verified as a new type of dynamic bonds.\textsuperscript{48,49} An efficient amine exchange process would happen when an amino-yne adduct is reacted with another excessive amine (Scheme 8). This process is similar to the transamination reaction commonly mentioned in dynamic covalent polymer network (DCPN) field. However, the former has less steric hindrance due to the absence of methyl substituent, leading to the faster dynamic exchange process than the latter. Polymer degradation was also realized by taking advantages of the dynamic characteristic of enamine bonds. The polymer chains were disassociated gradually after the addition of excess monoamine, the $M_w$ of which decreased from nearly 48 000 to 1 000 at 60 °C within 48 h. In addition, by taking advantage of dynamic nature of enamine groups, Lin et al. designed and prepared a vitrimer by amino-yne click polymerization (Figure 5).\textsuperscript{103} Compared with the referenced vitrimer BPAE-ATH produced by amine-acetoacetate condensation, the resultant vitrimer network BPAE-PTH showed a faster dynamic exchange as verified by Arrhenius analysis, and possessed superior mechanical properties,
which was attributed to the absence of byproduct such as water molecules, thus reducing the network defects. As a result, a uniform transparent polymer film was obtained by pressing the BPAE-PTH sheet at 130°C for 60 min. This work provided a powerful tool for the preparation of DCPN.

**Scheme 8. Comparison between Common Transamination Process in DCPN and Amine Exchange Process in Amino-Yne Click Polymerization**

The vinyl moiety produced by the X-yne click reaction is not just a structural linker for connecting the repeat units together but an important functional unit, which generally has both *cis*- and *trans*-configuration. Although our groups and others have endeavored on stereochemistry control of vinyl bond and stereoselective polymerizations have been successfully established, the impact of stereoselectivity is scarcely taken into account when studying polymer functionalities. Actually, the *E/Z*-isomerization can affect the packing mode of polymer chains so as to affect the mechanical and thermal properties of polymers. For example, PVS with high content of *cis*-isomer (80%) was verified to be semicrystalline according to the wide-angle X-ray diffraction (WAXD) analysis and differential scanning calorimetry (DSC) test. The degree of crystallinity decreased with the decreases of content of *cis*-isomers. However, when the value was below 53%, the samples were completely amorphous together with significantly reduced mechanical properties.
Furthermore, an intriguing configuration interconversion of the adduct of 3-butyn-2-one and aniline was observed in various solvents with different polarities. The relationships between stereoregularity of polymers and their functionalities are still obscure. Figuring out it and making it helpful for practical applications are of great importance.

![Amino-yne click reaction](image)

**Figure 5.** Illustration of the BPAE-PTH vitrimer dynamics and its Arrhenius analysis compared with BPAE-ATH, together with graphic illustration of hot-press reprocessing process.

### 4. Conclusions and Prospects

In this Perspective, we put forward a new concept of X-yne click polymerization, in which the polymerization is more efficient than the typical azide-alkyne click polymerization, and could be carried out under milder conditions, and the X refers to a new kind of monomers that are more benign and safer than the azide one, which includes thiols, alcohols and amines and other environmentally friendly and sustainable ones. The progresses in X-yne click polymerizations, especially the thiol-yne, hydroxyl-yne and amino-yne click polymerizations are accounted, their applications in preparation of functional polymeric materials are also briefly summarized and their challenges and opportunities are also discussed in detail. Thanks to the fascinating “click” characteristics, X-yne click polymerization will be eventually developed into a power tool for the
synthesis of polymers with unique structures and advanced functionalities, which will find diverse applications in optoelectronic, sensing and biological fields.

Meanwhile, although encouraging progresses has been made, the field is still in a developing stage, with many challenges yet rich opportunities awaiting to be addressed and grasped. Subsequent research directions should include the expansion of monomer scope beyond existing building blocks and substituents, development of novel polymerization methodologies based on other highly efficient organic reactions, precise regulation of the structures and configurations of polymers, and further clarification of the structure-property relationship. What’s more, we cannot stop at the development of the reaction itself, but should actively explore its functionality so as to broaden the applications. It is hope that this Perspective can draw more attention on X-yne click polymerization, making its advantages to be fully utilized and applied in more research fields.

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