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INVITED REVIEW

Click Chemistry in Macromolecular Design: Complex Architectures from Functional Polymers

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Abstract

This contribution reviews the applications of click chemistry reactions in design and synthesis of various macromolecular architectures that hold key aspects in polymer science. By considering the emerging concepts that shape how synthetic polymer chemistry and macromolecular engineering utilize 'reactions' in 'fabrication', in the last decade, the click chemistry methodologies have been pioneered the chemical approaches that allow to access diverse complex macromolecules. The common and leading features of click chemistry reactions rely on efficient, fast, selective and easy to implement chemical transformations giving very high to quantitative coupling efficiencies. These are essential virtues that provide triumphing in macromolecular engineering, since the building blocks are usually large polymer chains. For the efficient building of complex macromolecules via click reactions, properly functionalized polymers are key components in which special design is required to successful installation of 'clickable' reactive groups on polymer end groups or side chains. In this report, the synthetic methods encompassing various click chemistry reactions in fabrication and applications of a range of complex macromolecular architectures have been reviewed.

Keywords Click chemistry · Complex macromolecular architectures · Functional polymers · Polymer modification

1 Introduction

The complex polymer architectures including block copolymers, star polymers, graft or comb polymers and several other polymeric systems constitute important research areas of polymer chemistry [1]. These macromolecular structures have been in interest in material applications, since the unique structures of such architectures possess significantly different properties than the individual polymer components. Especially in solution state, different polymer architectures show self-assembly into high order three-dimensional structures that bring important attributes in colloid and interface science. Chemically different polymers may coordinate into structures that can bring distinct molecular composition and physical characteristics in solid state, as well as unusual solution dynamics [2].

A large set of chemical methodologies have been utilized in design and synthesis of complex polymeric architectures [3]. Although these structures exhibit great promise in material applications, the design and fabrication strategies are not usually straightforward and require through-going synthetic analysis and implementation. Important aspects, such as careful evaluation of chemical and physical properties of polymer components, efficient installation of reactive functionalities on polymer chains and successful coupling of building blocks into high order molecular structures are required to achieve desirable properties of fabricated materials. In this sense, efficient chemical reaction tools have great relevance to synthetic methods of macromolecular synthesis.

Generally accepted click chemistry methodologies include a set of highly efficient chemical reactions. These reactions possess and require various experimental conditions such as, catalyst-free or metal catalyst aided reaction coordinates, thermal or UV activations, reversible or irreversible reaction mechanisms, etc. In planning the effective macromolecular synthesis, these different reaction conditions could be useful while deciding the optimum production process. A set of lead advantages and limitations of various click reactions in macromolecular engineering are summarized in Table 1.

The most common example is referred as the copper(I)-catalyzed alkyne-azide cycloaddition (CuAAC) click reaction

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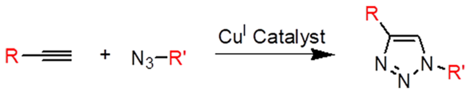
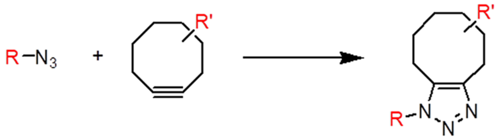
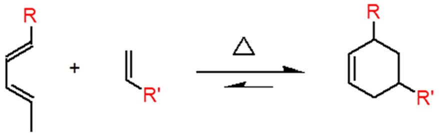
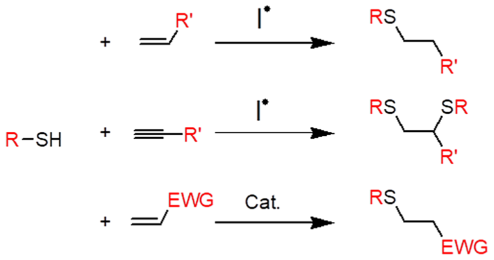
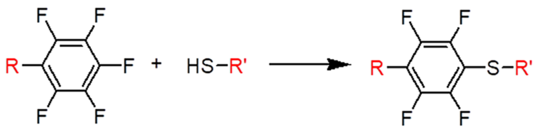
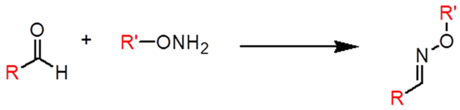
Table 1 Main advantages and limitations of various click reactions in macromolecular synthesis

Click reaction[a]	Mechanism	Advantages	Limitations
CuAAC		High selectivity, rapid and quantitative transformations, stability, orthogonality	Need to use (toxic) metal catalyst. Removal of the catalyst
SPAAC		Selectivity, high reactivity and biocompatibility. No metal catalyst is required	Strained alkynes are not so common and expensive materials
Diels–Alder		Reversibility of the reaction. Most of the time no byproduct formation	Activation through heating. Relatively prolonged reactions times
Thiol–ene/thiol–yne		Simple experimental conditions. Fast reaction kinetics	Low coupling efficiencies. Thiols are prone to many side reactions and have low self-stability
PFTR		High reactivity and very fast transformations	Not selective between alcohol, amine and thiol nucleophiles
Oxime click		High reactivity and high conversions	Complex synthetic routes to achieve hydroxylamines

[a] *CuAAC* copper(I)-catalyzed alkyne-azide cycloaddition, *SPAAC* strain-promoted alkyne-azide cycloaddition, *PFTR* para–fluoro–thiol reaction

that employs complementary alkyne and azide functional building blocks [4, 5]. CuAAC reactions have gained prevalent utilization in polymer science and have been employed in fabrication and functionalization of diverse polymeric materials [6–17]. Diels–Alder reactions constitute another important click methodology that proceeds under metal catalyst–free reaction conditions and the reaction kinetics are usually controlled with thermal effects [18–25]. This atom economic cycloaddition-based click approach has found widespread applications in synthesis of various macromolecular constructs [18, 23, 26–31]. Another highly efficient click chemistry methodology is based on the addition reactions of thiols with various alkene and alkyne substrates. These reactions are referred as thiol–ene and thiol–yne click reactions and have gained acceptance as efficient, reliable and robust procedures in fabrication and applications of functional polymeric materials [32–39]. Click chemistry methodologies are not restricted to these common reactions and various other concepts portraying 'click' features have been utilized in procuring of polymeric materials. For example, thiol-para fluoro click reaction [40], Ugi, Passerini and Biginelli multicomponent reactions [41, 42] and sulfur(VI) fluoride exchange (SuFEx) [43] are new family of click chemistry-related transformations that have gathered utilization in synthesis various macromolecular constructs.

In the current manuscript, the applications of click chemistry-based methodologies in synthesis of complex polymer structures were surveyed (Fig. 1). By considering the synthetic aspects, the examples in design and synthesis of reactive polymers and further click coupling into higher macromolecular structures have been reviewed. Since there are comprehensive studies and review articles that summarize the macromolecular applications of click chemistry reactions where mainly small molecules are employed in various aspects (Table 2), in the current study, we mainly focused on the examples that utilize reactive polymers as building blocks in complex architecturing. Thus, macromolecular constructs prepared by click coupling of complementary

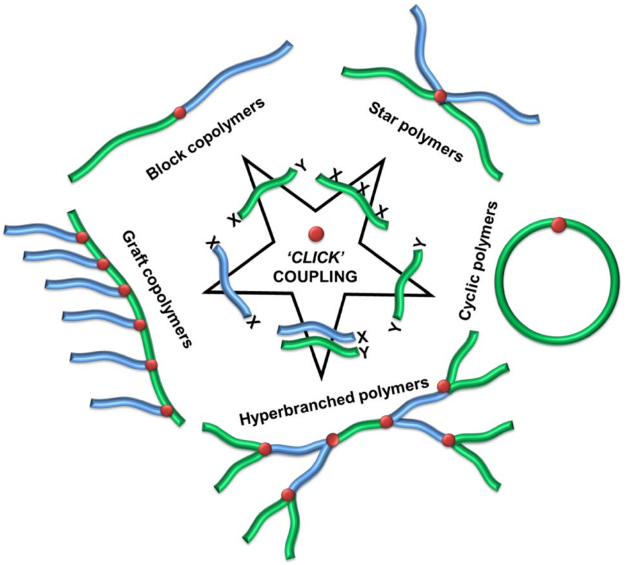


Fig. 1 Various macromolecular architectures that employ 'clickable' reactive polymeric building blocks

functional small molecule monomers or grafting clickable polymers onto reactive non-polymeric scaffolds were not included.

2 Complex Polymer Architectures Via Click Chemistry Reactions

2.1 Block Copolymers

Block copolymers constitute an essential part of complex polymer architectures and in their diversities, they are potential building blocks in formation of self-assembly driven nano- and micro-structures [48, 49]. The applications of block copolymers span from industrial compatibilizers and dispersants to biomedical applications as drug nano-carriers [50, 51]. These applications necessitate good control over chemical and physical properties of block copolymers during fabrication; which in return make architecting tools important to impart desired functionality. Apart from this, due to the limitations of conventional and controlled radical polymerization techniques in the synthesis of block copolymers with chemically different building segments, click chemistry-based architecturing of functional polymers remains as efficient and convenient engineering tools.

Starting from the introduction of the click chemistry concept into polymer chemistry, the click reactions have been employed in the synthesis of diversely-structured block copolymers in conjunction with controlled radical polymerization (CRP) techniques [52, 53]. Functional initiators and chain transfer agents employed in CRP methods such as, reversible addition-fragmentation chain transfer (RAFT) polymerization, atom transfer radical polymerization (ATRP) and nitroxide-mediated radical polymerization (NMP) allow direct installation of clickable reactive groups at polymer chain ends [54]. This strategy assures, if not the placement of such functionalities on each chain ends, but the maximum available installation that play a crucial role in clicking of complementary functional polymer chains with high coupling efficiency.

The installation of either azide or alkyne groups on chain transfer agents (CTA) used in RAFT polymerization is a common strategy that allows the synthesis of block copolymers via CuAAC click reaction [55]. These clickable groups are orthogonal to a large set of other organic functional groups and allow successful RAFT polymerization in case of using functional group-containing monomers. CuAAC click coupling enables highly efficient attachment of individual polymer chains via formation of five-membered triazole junctions. In an early example, Stenzel and co-workers prepared poly(styrene)-*b*-poly(vinyl acetate) block copolymers by utilizing two different CTAs that carry either azide or alkyne moieties [56]. To assure the prevention of acetylene groups in interfering with radical species, a trimethyl silyl

Table 2 Some of recent literatures that focus on click chemistry applications in polymer science

Running title	Scope of the review	Publication year	Refs.
Click polymerization: the aurora of polymer synthetic methodology	Recent progress on click polymerizations, with focus on the CuAAC click reaction	2017	[44]
Polymer nanocomposites via click chemistry reactions	General overview on the applications of click reactions in design and fabrication of polymer nanocomposites	2017	[15]
"Click" chemistry in polymeric scaffolds: bioactive materials for tissue engineering	Accounts several kinds of polymeric scaffolds prepared/modified via "click" reactions, with emphasis on their biomedical applications	2018	[45]
Click and click-inspired chemistry for the design of sequence-controlled polymers	Recent advances in click chemistry-mediated synthesis of sequence controlled polymers	2017	[46]
Metal-free click chemistry reactions on surfaces	The backgrounds and applications of metal-free click reactions for the modification of surfaces	2015	[47]

protection of these groups was performed before polymerization. This strategy was also employed in the synthesis of thermo-responsive block copolymers by using CTAs of azido- and alkyne-terminated trithiocarbonates [57]. However in this case, the alkyne groups were not protected and were reported to be stable during RAFT process.

ATRP is another widely applied CRP technique that allows direct access to diverse block copolymer libraries by combination with CuAAC click reaction. Common strategies include the polymerization of monomers initiated with azide or alkyne functional initiators that provide clickable end groups at polymer chains. In order to prevent the participation of the acetylenic units into polymerization, the alkyne functional initiators are usually protected with suitable protecting groups prior to the ATRP process [58, 59]; though there are examples that implement ATRP using initiators bearing unprotected alkyne functionalities [60–62].

The end group modification of ATRP polymers with CuAAC clickable azide groups is a key synthetic step that impart click coupling of these reactive polymers with complementary alkyne functional macromolecules. This modification can be carried out by nucleophilic substitution of end-chain haloalkyl groups with azide anions to lead ω-functional polymers. The high yielding functionalization of chain end groups however require ideal reaction conditions [63].

In a study, *α*,*ω*-diazido-terminated polymers were prepared by Matyjaszewski and co-workers by employing a bifunctional ATRP initiator during polymerization and subsequent post-polymerization azidation steps [64]. CuAAC click coupling of synthesized homotelechelic polymers with a dialkyne functional chain extender resulted in the formation of multi-segmented (ABA) block copolymers (Fig. 2). In another study, ABA'-type triblock asymmetric amphiphilic copolymers were reported by Zhang and co-workers by a combined ATRP and CuAAC click route [65]. Synthetic steps included the ATRP of styrene monomer with a poly(ethylene oxide) monomethylene ether (MPEO) based macro-initiator. The resulting block copolymer was azidated and subsequently conjugated with an alkyne-functional MPEO polymer.

Block copolymer synthesis by combining different CRP techniques could offer a convenient route. This is especially prevalent when the controlled radical polymerization efficiency of a monomer is low with a certain technique, but not with another CRP method. Examples include CuAAC click synthesis of block copolymers from azide or alkyne end-functional polymers obtained via RAFT and ATRP techniques [66–68].

Block copolymers containing π-conjugated polymer chains have been in interest in semiconducting material applications, such as organic photovoltaics, light emitting diodes and field-effect transistors. The structures of the polymer blocks composed of chemically different segments may induce phase separation of electron donor and acceptor groups, thus improving the charge transfer [69]. The CuAAC click chemistry mediated coupling of bisalkyne functional poly(3-hexylthiophene) polymers with ATRP-generated azide functional polystyrene was reported by Urien et al. [70]. The installation of acetylene units at π-conjugated polymer chain ends was achieved by Grignard metathesis polymerization (GRIM) using alkynyl Grignard reagents

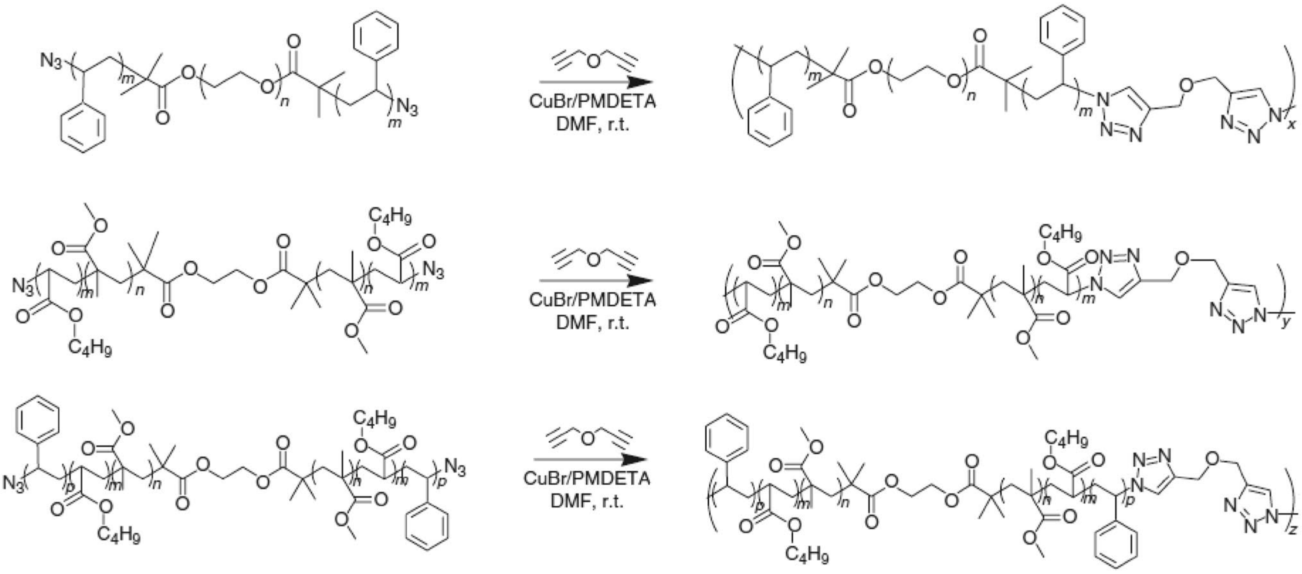


Fig. 2 CuAAC click-mediated synthesis of various multisegmented block copolymers by employing α,ω-diazido-terminated polymers. Adapted from [64] with permission. Copyright © 2007 by CSIRO Publishing

and subsequent end group modification. In a similar manner, Verduzco and co-workers reported the preparation of amphiphilic poly(alkylthiophene) block copolymers via CuAAC reaction [71]. This approach included the installation of alkyne units at one polymer chain ends of poly(3-alkylthiophenes) polymer via esterification. In a later study, same group reported CuAAC click coupling block copolymer formation of two different conjugated polymers [72].

In the click chemistry-mediated architecturing of block copolymers, the nitroxide-mediated radical polymerization (NMP) has drawn less attention than RAFT and ATRP methods. On the other hand, successful implementation of CuAAC click reaction in styrenic block copolymer synthesis by using functional NMP initiators and post-polymerization modification techniques were reported [73, 74].

In an intriguing example of block copolymers synthesis from polydiene building blocks, Hadjichristidis and co-workers reported the synthesis of cyclic and multiblock polystyrene-*b*-polyisoprene copolymers by combining CuAAC click reaction and anionic polymerization (Fig. 3) [75]. A unique strategy of using protected acetylene-functionalized lithium initiator was employed in polymerization. The living anionic polymerization of styrene and isoprene monomers provided anionic end groups, which were later transformed into alkyl bromide and azide functions. After deprotecting the acetylenic units, CuAAC click reaction provided either cyclic or multiblock copolymers depending on the reaction conditions. Protected acetylene-functionalized organolithium species were later utilized in anionic polymerization to polyferrocenylsilanes [76]. CuAAC click-mediated block copolymers of polyferrocenylsilanes with various azide end group functional polymers were successfully reported demonstrating the efficiency of anionic polymerization in placement of clickable functionalities at polymer chain ends. A conceptually similar study reports the living nickel(II)-mediated polymerization of carbodiimides for the synthesis of alkyne end functional coiled polymers [77]. Subsequent CuAAC click coupling of such polymers with azide end-functional polystyrene and polyethylene glycol polymers resulted in helical-*b*-coil block copolymers which show interesting nanofibular morphologies in filmed state and when subject to specific conditions.

Macromolecular structures containing building chains of cyclic monomers constitute an important sub-discipline in macromolecular engineering. Click chemistry approaches in combination with ring opening polymerization (ROP) methods provide handy tools in design and synthesis of block copolymers with self-assembly properties that play multifaceted roles in polymer chemistry, nanotechnology and colloids and interface sciences. Chemically different cyclic monomers result in structurally diverse polymer blocks that may possess for example, biodegradable and biocompatible properties, peculiar change of structural conformations, thermosensitive properties and phase separation. From synthetic point of view, ROP usually provides easy installation of reactive functional groups at polymer chain ends, since the polymerization reactions can be initiated with functional nucleophilic initiators and such functionalities are preserved after polymerization. In addition to this, post-polymerization modification techniques could provide tailoring of reactive ROP polymer end groups for installation of clickable functionalities for the later macromolecular engineering (Fig. 4).

In this regard, CuAAC click reaction has been extensively utilized in block copolymer formation of ROP polymers with diversely other polymeric systems. Cyclic monomers that have been employed in ROP polymerization initiated either with azide or alkyne functional nucleophilic initiators include, *N*-carboxyanhydride [60, 79], ε-caprolactone [78, 80, 81], and D,L-lactide [82, 83] monomers. Post-polymerization end group modification approaches of ROP polymers on the other hand include, alkyne decoration of poly(ε-caprolactone) [84] and azide functionalization of polydimethylsiloxane [85] and poly(2-ethyl-2-oxazoline) [78] polymers. In a unique example, ring opening metathesis polymerization (ROMP)-mediated clickable polymers were synthesized via post-polymerization modification and subsequently used in CuAAC click coupling block copolymer formation with azide functional PEG polymer [86].

Dendronized block copolymer conjugates are interesting macromolecular structures that demonstrate therapeutic

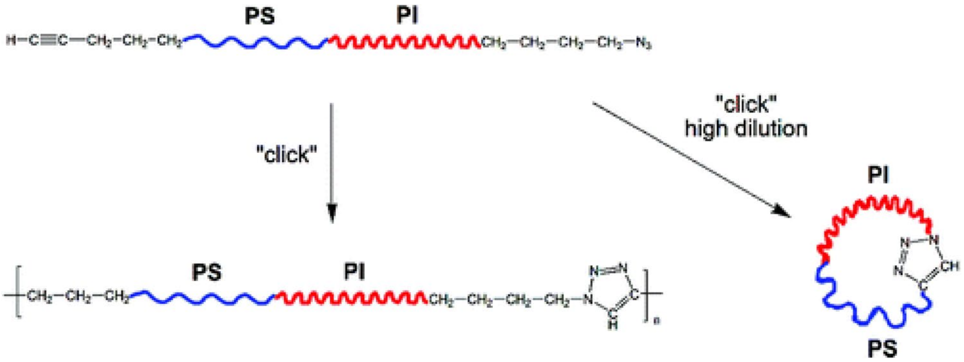


Fig. 3 Combining living anionic polymerization and CuAAC click reaction for the synthesis of cyclic or multiblock copolymers. From [75] with permission. Copyright © 2011 by the American Chemical Society

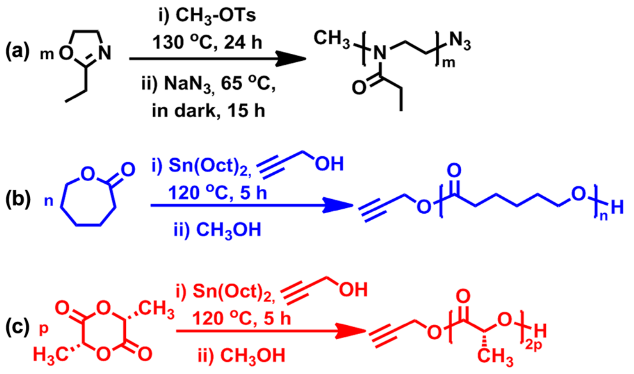


Fig. 4 Installation of CuAAC clickable reactive end groups onto ROP-mediated polymers via **a** post-polymerization modification; **b**, **c** functional nucleophilic initiation. From [78] with permission. Copyright © 2018 by the Express Polymer Letters

value in biomedical applications. Linear polymers with clickable end groups provide convenient fabrication of such polymeric systems since well-defined dendritic structures allow the placement of complementary functional clickable groups at dendron focal groups. In this sense, CuAAC click reaction was shown to be prospering in conjugation of linear polymer chain ends with various dendritic structures [87–89].

A promising and effective click chemistry approach towards block copolymer synthesis relies on Diels–Alder (DA) and hetero Diels–Alder (HDA) cycloaddition reactions [19]. This strategy includes the installation of complementary diene and dienophile functional groups on linear polymer chain ends that allow coupling of building blocks by [4+2]-cycloaddition junctions. HDA reaction is a variant of DA reaction in which in [4+2] π-electron system, either diene or dienophile contains a heteroatom, presumably oxygen, nitrogen or sulfur. The common DA and HDA clickable reactive groups include anthracene, maleimide, furan, cyclopentadiene and their derivatives. These groups are usually attached to CRP and ROP initiators that allow the direct synthesis of linear polymers with DA and HDA clickable groups. The efficient conjugation of polymer blocks require careful control of thermal conditions since DA reactions are thermoreversible and especially at high temperatures, reverse retro DA reaction competes with forward cycloaddition. DA-based click approaches provide orthogonal design of macromolecular structures with other click-based concepts, such as CuAAC and thiol–ene reactions. These "double-click" or "triple-click" reaction methodologies allow fast and efficient construction of various macromolecular topologies that find important applications in manifold areas, such as inorganic–organic hybrids and biomolecular conjugations [90].

Hizal and co-workers have elaborated DA reaction in synthesis of various macromolecular architectures including linear block copolymers [21, 91]. The group, for example reported the synthesis of well-defined polystyrene/PEG block copolymers employing anthracene functional polystyrene and maleimide functional PEG building blocks (Fig. 5) [21]. It was shown that the coupling efficiency of DA reaction was higher than 92%, demonstrating the power of DA reaction in conjugation. In a recent example, Hsu et al. reported the enantiomeric block copolymers of polylactide and polyethylene glycol by the chain extending Diels–Alder reaction [92].

DA click-based construction of diblock and triblock dendron-polymer conjugates was reported by Sanyal and co-workers [93]. Linear polymer-biodegradable polyester dendron blocks were efficiently synthesized by thermally driven cycloaddition of maleimide functional PEGs and anthracene core group containing dendrons with various generations. In a different study, the group utilized cascade CuAAC and DA double-click reactions to construct pH-degradable dendron functionalized poly(2-ethyl-2-oxazoline) polymers (Fig. 6) [94].

Barner-Kowollik and co-workers pioneered the macromolecular engineering of RAFT-mediated polymers towards hetero Diels–Alder click-based building of various structures, including block copolymers. The group reported the highly efficient HDA cycloaddition conjugation of RAFT dithioester groups with macromolecules containing reactive cyclopentadiene or 2,4-hexadiene-terminated end caps (Fig. 7). The conjugation reactions were demonstrated to proceed in a very rapid fashion under ambient temperature and atmosphere conditions. This strategy was utilized in the synthesis of polystyrene/poly(ε-caprolactone) [95],

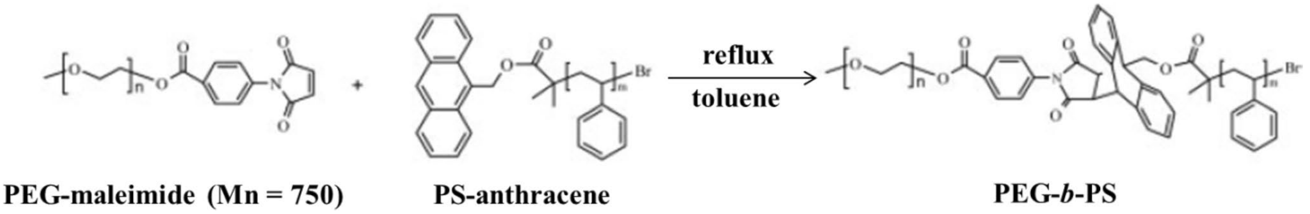


Fig. 5 Block copolymer synthesis from different polymers containing DA clickable end groups. Adapted from [21] with permission. Copyright © 2006 by Wiley Periodicals, Inc

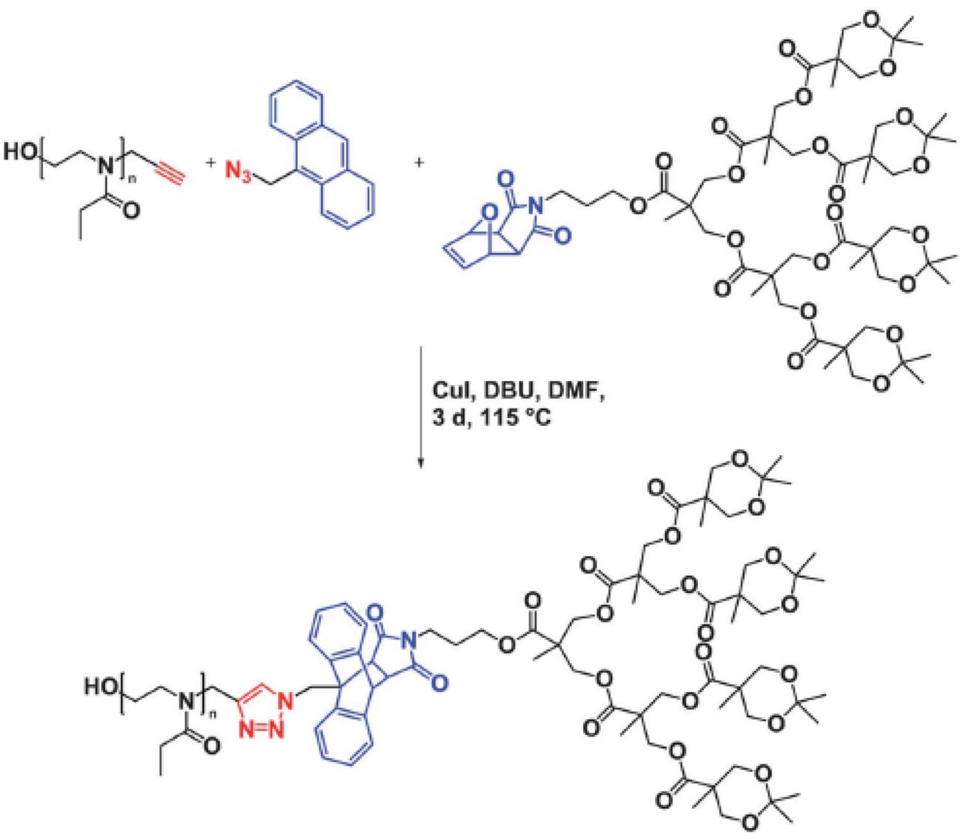


Fig. 6 DA and CuAAC double-click strategy towards linear polymer-dendron conjugates. From [94] with permission. Copyright © 2013 by The Royal Society of Chemistry

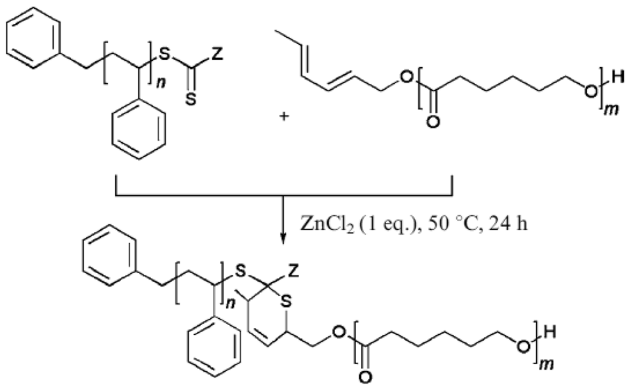


Fig. 7 Efficient hetero Diels–Alder conjugation of RAFT-mediated polymers with diene end-capped macromolecules. Adapted from [95] with permission. Copyright © 2008 by The Royal Society of Chemistry

polystyrene/poly(isobornyl acrylate) [96], polyethylene/poly(isobornyl acrylate) [97] block copolymers and amphiphilic diblock copolymers with a temperature switchable linkage [98].

Though, thiol–ene and thiol–yne click reactions have found numerous applications in polymer chemistry, they found limited practice [99] in the synthesis of block copolymers. The challenges [100] regarding the efficient coupling of large polymer chains remain as drawbacks during successful implementation of thiol–ene reactions and need more elaborated research.

Several other chemical reactions associated with click chemistry concept have been successfully employed in synthesis of block copolymers. These include the oxime click reaction [101, 102], Ugi multi-component reactions [103] and nitrile *N*-oxide based [104] chemical conjugation strategies.

2.2 Graft/Brush/Comb Copolymers

A considerably important application area of click chemistry methodologies in macromolecular engineering imparts the synthesis of graft polymers and related brush and comb structures. Attaching structurally different polymer chains onto side chains of polymer backbone is a way of tuning material properties that might be important in various applications [105]. The main approaches in the synthesis of such polymer architectures rely on ‘grafting from’, ‘grafting through’ or ‘grafting onto’ strategies. The prospect of grafting onto strategy is applied in conjugation of polymeric building blocks and is a promising method; since it allows the preparation of polymer blocks separately in a controllable manner. The main drawback of grafting onto strategy is the often encountered low grafting density which requires highly efficient and operationally simple synthetic routes for conjugation. Versatile click reactions have found wide applications in attachment of functional polymers onto side chains of complementary functional polymers.

The main chain polymers carrying CuAAC-clickable side chain groups could be obtained via several CRP and post-polymerization modification techniques [106]. In an early example, Matyjaszewski and co-workers reported the grafting of alkyne-functional PEG polymer onto ATRP-mediated azide side groups containing poly(glycidyl methacrylate)-*b*-poly(methyl methacrylate) block copolymers (Fig. 8) [107]. The azide moieties were obtained via azidation of glycidyl groups. It was shown that the grafting efficiency was up to 75% in most ideal catalyst, temperature and reactant stoichiometry conditions.

One of early studies of CuAAC-mediated polymer grafting employed the RAFT-mediated synthesis of propargyl methacrylate and vinyl acetate block copolymers [108]. During the polymerization, the acetylenic units were protected in order to avoid their participation into growing free radicals. As an alternative strategy, efficient azide group installation on RAFT polymer side chains could be carried out as a post-polymerization functionalization step [109].

The ROP-mediated side chain functional polymers have been extensively investigated as effective conjugation platforms in CuAAC-mediated polymer grafting. Various main chain macromolecules including polymers of cyclic ε-caprolactone [110–113], trimethylene carbonate [114] and oxazoline [115] monomers were grafted with different polymers, i.e. poly(ethylene oxide), poly(*N*-isopropylacrylamide), poly(D,L-lactide) and long-chain fatty acids. Installation of either azide or alkyne functional groups during polymerization or attaching such functionalities in post-polymerization stage could be successfully implemented.

In a recent example, ROMP polymers carrying azide side chains were utilized in grafting of poly(ethylene glycol) and/or poly(ε-caprolactone) polymers for the synthesis of comb-like graft copolymer structures (Fig. 9) [116]. According to the results, a stoichiometric amount of alkyne-terminated polymer was adequate to ensure the complete conjugation.

The naturally occurring polymers are indisputably important materials in various applications. A majority of polysaccharides (i.e. cellulose and hemicellulose, chitin and chitosan, amylose, xylan, dextran and several gums) and other biopolymers are plant, algae or bacteria originated which they comprise focal point in green technologies. The leading properties of naturally occurring polymers such as, renewability, biodegradability, biocompatibility and nontoxicity make them ideal candidates in diverse applications. However, most of the applications require chemical modification of such polymers, especially to overcome the solubility-related limitations. Macromolecular engineering of biopolymers is heavily based on the grafting of small molecule or polymers onto side chains of backbone structure. In this sense, versatile CuAAC-mediated click strategies have found applications in grafting of polymeric precursors to clickable side-chain functionalities [117]. The installation of clickable groups is carried out by different methods such as, alkynation of backbone hydroxyl groups [118, 119], periodate oxidation/reductive amination with propargyl amine [119, 120] and azidation [121–124]. Different synthetic polymers having complementary clickable functionalities have been utilized in grafting with imposing key duties such as, increasing water or organo solubility and bringing amphiphilicity to polymer structure.

Graft copolymers are important materials in industrial applications and are used as impact-resistant plastics, thermoplastic elastomers, viscosity improvers, compatibilizers and emulsifiers [125]. An intriguing approach relies on the installation of clickable functionalities at side chains of commercial linear polymers and subsequent conjugation of different polymers onto these groups. This approach provides fine tuning of material properties by altering the

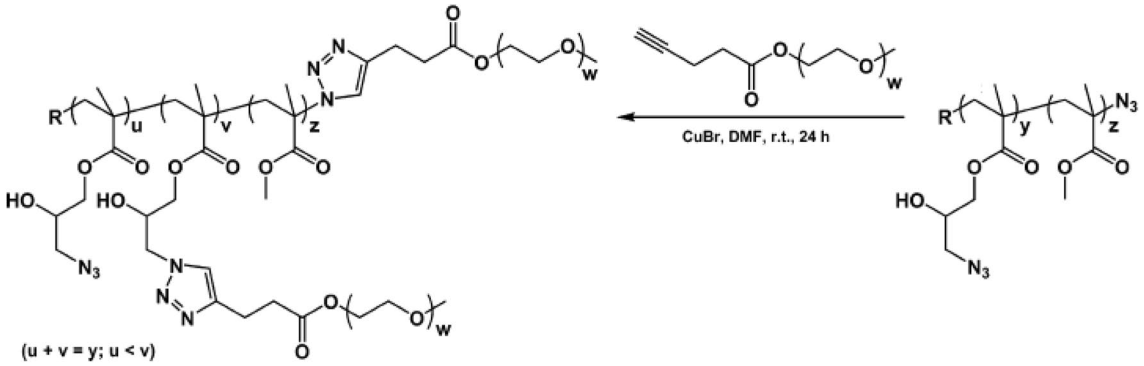


Fig. 8 CuAAC click mediated grafting of alkyne functional polymer onto azide side groups of main block copolymer. Adapted from [107] with permission. Copyright © 2007 by the American Chemical Society

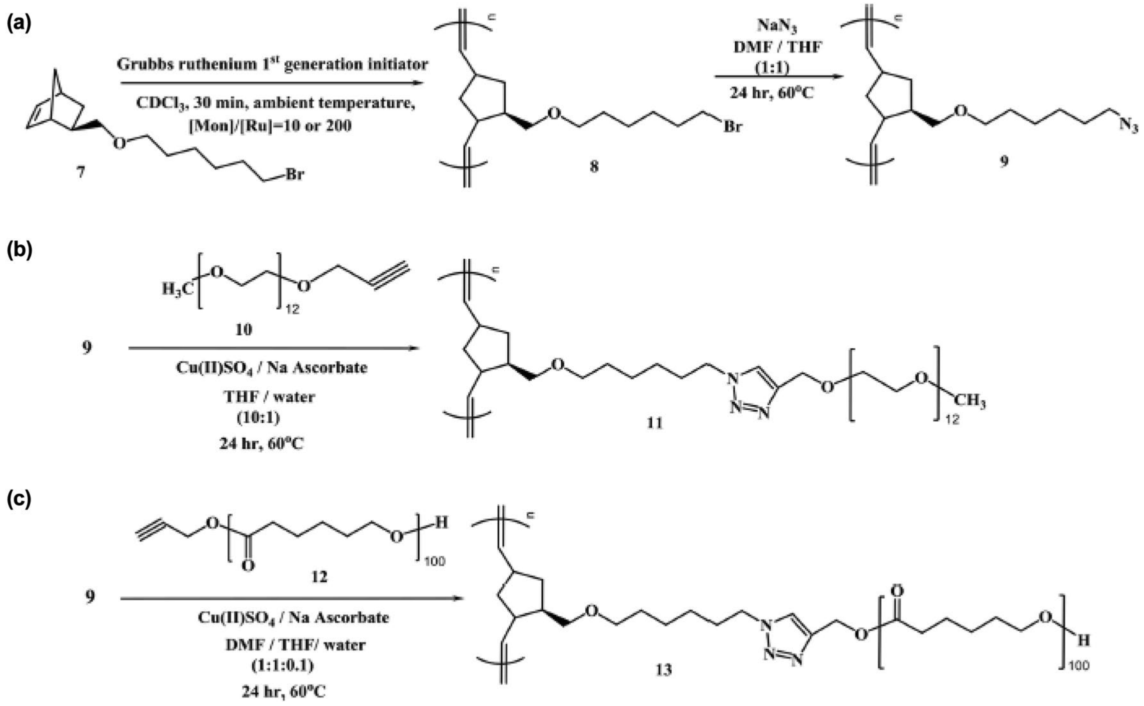


Fig. 9 **a** Synthesis of clickable ROMP polymers and **b**, **c** subsequent CuAAC-mediated click polymer grafting. From [116] with permission. Copyright © 2015 by Wiley Periodicals, Inc

grafting density via controlled attachment of reactive side chain groups. Tasdelen and co-workers exploited CuAAC click reaction in synthesis of graft polymers from commercial polystyrene-poly(vinyl chloride) [126] and chlorinated polypropylene polymers [127]. The approach included the first attachment of azide groups at side chains and subsequent grafting conjugation with alkyne functional polymers. A similar strategy was employed by Lee et al. for grafting of hyperbranched polyglycerol onto poly(vinyl chloride) to structurally enhance its self-plasticization [128].

The CuAAC-mediated grafting strategy has also been utilized in the synthesis of all-conjugated comb copolymers [129], ABA-type block-graft copolymers [130], aliphatic polyesters with hydrophilic side chains [131] and polysulfone-based amphiphilic graft copolymers [132, 133].

Diels–Alder click chemistry-based synthesis of graft polymers have been extensively studied by Hizal and co-workers. The group has mastered in DA-based tailored architecturing of functional polymers in combination with various FRP-CRP, ROP and ROMP methods. In addition to common acrylic/methacrylic and styrenic main block polymers [24], poly(oxanorbornene)s [25], polyurethanes [134] and polycarbonates [135] with DA-clickable side groups have been employed in graft polymer synthesis. Successful implementation of CuAAC/DA-based sequential double click [136, 137] and CuAAC/DA/NRC (nitroxide radical coupling)-mediated triple click reactions [138] in graft polymer synthesis was also reported by the group.

The grafting onto strategy via a combination of RAFT polymerization and HDA cycloaddition was employed by Barner-Kowollik and co-workers in highly efficient synthesis of comb polymers [139]. The installation of *trans* hexa-2,4-dienyl moieties during RAFT polymerization provided HDA-clickable diene functionalities at side chains. Benzyl pyridin-2-yldithioformate RAFT polymer end moieties were subsequently used as dienophile counterparts during grafting conjugation. The reactions were implemented at 50 °C in 12–24 h reaction times yielding 75–100% conjugation efficiencies depending on the grafted polymer chain lengths.

In a recent study, Gillies and co-workers extended the scope of DA-based polymer grafting to poly(isobutylene-*co*-isoprene) rubber functionalization. A three-step installation of different dienes on rubber backbone and subsequent DA grafting with maleimide-functional PEO or PSt has provided facile synthesis of new rubber derivatives with tunable mechanical and adhesion properties [140].

Modular synthesis of side chain dendronized polymers via DA click [28] and CuAAC-DA double click reactions [141] was reported by Sanyal and co-workers. In the double click approach, efficient grafting of core-clickable dendrons with different molecular structures provided hetero-graft dendronized polymers (Fig. 10).

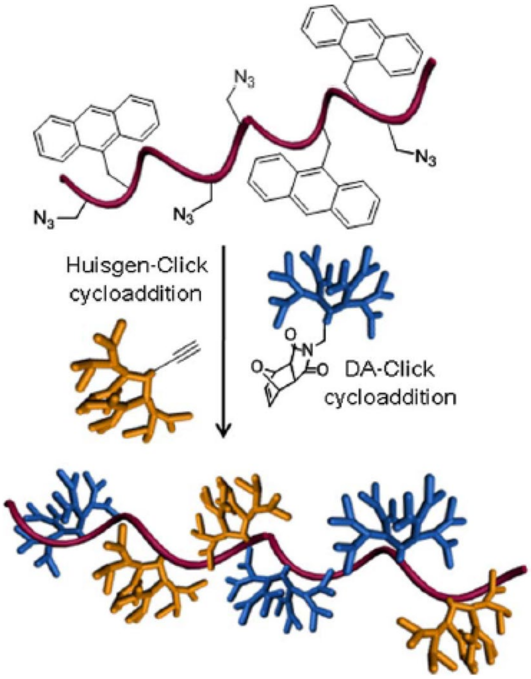


Fig. 10 CuAAC/DA based double click approach for the synthesis of hetero-graft dendronized polymers. From [141] with permission. Copyright © 2013 by Wiley Periodicals, Inc

Though scarce, thiol–ene [142] and para-fluoro-amine [143] based click approaches have been employed in synthesis of functional graft copolymers.

2.3 Cyclic Polymers

Due to their unique topological structures and distinct solution and bulk properties, cyclic polymers have attracted increasing attention in macromolecular design [144]. However, the synthetic task of cyclic polymer synthesis with high purity, high reaction conversion and controlled architecture is challenging. The main route to cyclic polymer synthesis relies on the ring-closure coupling of telechelic polymers chain ends, in which the conditions for cyclization are of significant importance. Restraining the production of substantial amount of linear counterparts or avoiding the knots or knots within the ring requires highly efficient coupling strategies in synthesis of such polymers. In terms of the controlled and highly dilute reaction conditions applied in ring-closure strategies, versatile click methods are undoubtedly handy tools.

CuAAC-mediated ring closure of telechelic polymers carrying clickable azide and alkyne end groups at chain termini is a common approach in synthesis of cyclic polymers. The examples combine ATRP [145, 146] or ROP [147] methods with subsequent post-polymerization modification to ensure the synthesis of well-defined clickable telechelic polymers (Fig. 11).

CuAAC click reaction provides highly efficient topological architecturing of cyclic polymers such as, bridged- and spiro-multicyclics [148] and heteroeight-shaped cyclic polymers [149]. Diverse applications of cyclic polymer synthesis via CuAAC reaction have recently been reviewed [150].

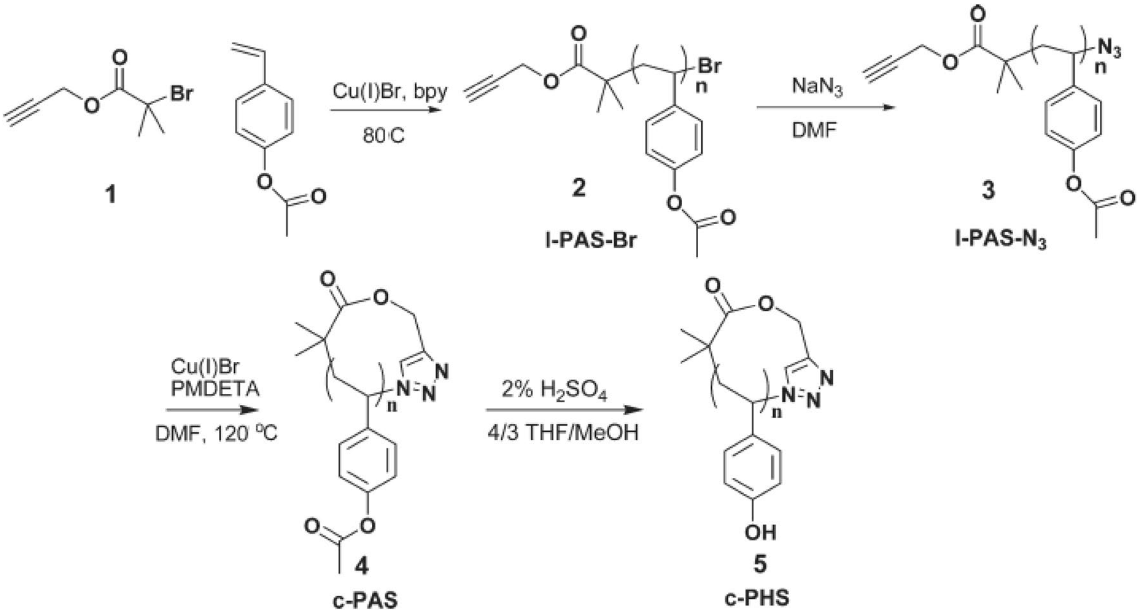


Fig. 11 An ATRP and subsequent end-group modification approach towards the synthesis of cyclic poly(4-acetoxystyrene) as a scaffold for further functionalization. Adapted from [145] with permission. Copyright © 2011 by the American Chemical Society

Wu, Zhang and co-workers have recently demonstrated an intriguing approach in ring-closure mediated synthesis of cyclic polymers [151–153]. The group employed the α,ω-homodifunctional linear polymers with azide end-groups in the self-accelerating double strain-promoted azide-alkyne click ring closure by employing dibenzo-1,5-cyclooctadiene-3,7-diyne linker.

Tunca and co-workers extensively studied the cyclic polymer topologies that employ various CRP, ROP and click methods [19]. In a study, they demonstrated the orthogonal Diels–Alder and CuAAC click reactions in preparation of cyclic homo and block copolymers [154]. The approach involved the first synthesis of well-defined linear precursors via a combination of ATRP and CuAAC-mediated end-group modification and subsequent DA-based ring closure (Fig. 12). In a similar study, Barner-Kowollik and co-workers reported the synthesis of high purity cyclic polymers by combination of ATRP and DA methods [155].

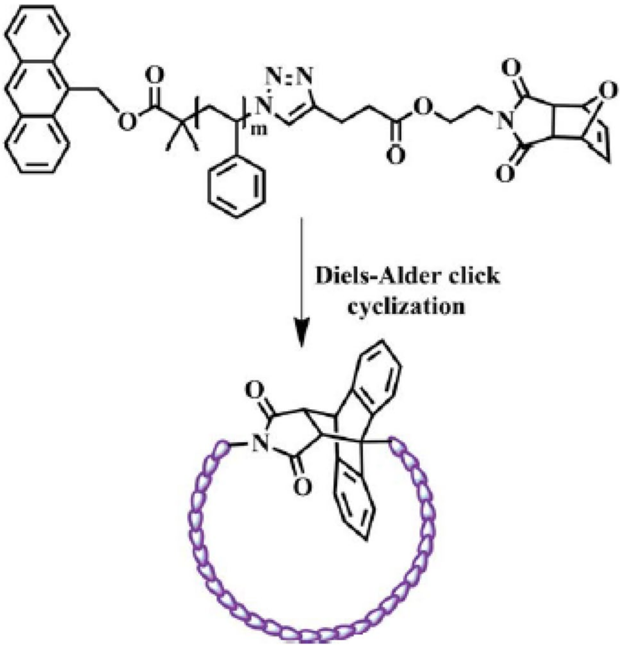


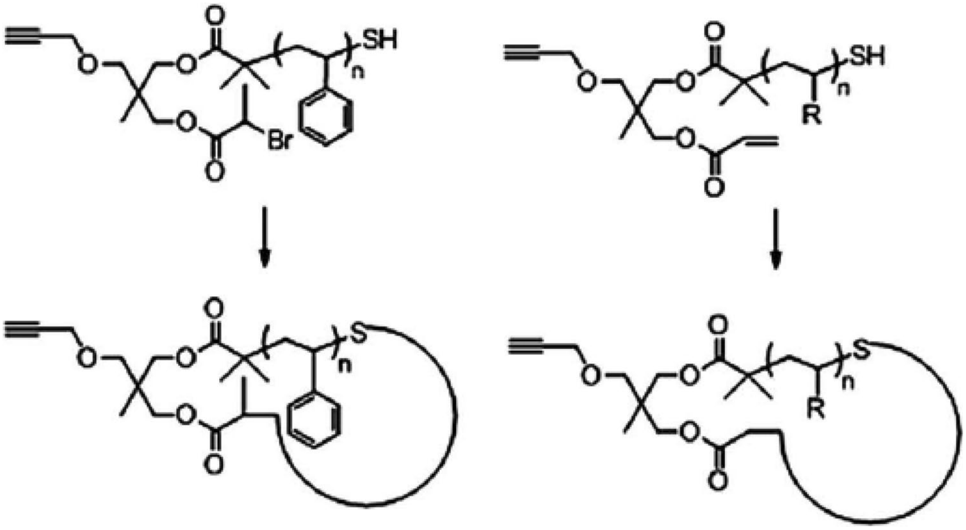
Fig. 12 Synthesis of cyclic polymers via DA click reaction. Adapted from [154] with permission. Copyright © 2010 by Wiley Periodicals, Inc

The efficiencies of thiol-X based reactions in ring-closure cyclization of RAFT-mediated polymers were investigated by Lu et al. [156]. The cyclization of functional polymers via thiol–ene and thio-bromo reactions was conducted in a one-pot fashion by aminolysis of RAFT end group and thiol–ene or thio-bromo coupling sequence (Fig. 13). According to the results, the optimum conditions for the thiol–ene cyclization provided ~ 80% cyclization of polymer chains whereas, thio–bromo reaction could only produce ~ 25% cyclic polymer.

2.4 Star Polymers

Star polymers, owing to their branched structures and compact-globular shapes, possess some of unique and attracting properties that are widely researched in macromolecular material engineering. Various methods have been used in synthesis of star polymers combining CRP and ROP techniques as well as, ionic polymerization methods. [157, 158] Especially by employing polymeric building blocks, the coupling reactions are very important in modular and defect-free synthesis of star polymers. Oftentimes, click chemistry methodologies accompany with aforementioned polymerization methods in post-polymerization functionalization or conjugation reactions [159]. Highly efficient, modular and orthogonal click reactions provide utility in design and

Fig. 13 Synthesis of functional macrocycles via thio-bromo and thiol–ene reactions. Adapted from [156] with permission. Copyright © 2013 by The Royal Society of Chemistry



synthesis of star polymers with different strategies such as, core-first, arm-first or coupling-onto approaches.

The early example of CuAAC click reaction in synthesis of miktoarm star polymers was reported by Monteiro and co-workers [160]. Miktoarm stars possess chain arms with different chemical composition. The approach included the attachment of azide end-functional ATRP-generated polymers onto a trifunctional alkyne core. Depending on sole introduction of homopolymers or successive addition of different azido polymers, miktoarm stars with different chemical architecture were obtained.

The judicious combination of CRP, ROP and CuAAC click reaction is an efficient strategy where star polymers with chemically different polymeric arms could be obtained [161, 162]. Such polymer architectures possess interesting solid state, interfacial, self-assembly and solution properties [163]. This concept was utilized by Pan and co-workers by combining ATRP, ROP and CuAAC reactions in the synthesis of structurally unique inverse-star block copolymers [164] and ABCD 4-miktoarm star polymers [165].

Matyjaszewski and co-workers employed a combination of ‘core-first’ and ‘coupling-onto’ strategies towards the synthesis of three-arm star block copolymers [166]. ATRP of polystyrene was conducted on a three-bromo functional core and after polymerization, bromo groups were converted into azide groups. Alkyne-terminated poly(ethylene oxide) chains were then coupled onto azide-terminated three-arm polystyrene.

Growing the arms directly from a polymeric core was implemented by Wang et al. [167]. A multi-azidated hyperbranched polyglycerol (HPG) was grafted with alkyne functional block copolymer. The synthesis of clickable copolymer involved the elegant combination of various polymerization and end-group modification techniques (Fig. 14).

Core-crosslinked star polymers are fundamental macromolecular constructs where they find important biomedical applications. This is especially prevalent when building the arm chains with stimuli-responsive properties [168]. Wiltshire et al. demonstrated the arm-first technique of star polymer synthesis employing core-crosslinking strategy [169]. CuAAC click coupling of azido-functionalized linear polystyrene onto core-crosslinked acetylene-functional polymer resulted in star polymers with brush-like arms (Fig. 15). The hydrolysis of degradable polycaprolactone segments in the later stage provided molecular brushes. In another application, polystyrene based core-crosslinked multiarm star block and multiarm star mixed-block copolymers employing CuAAC click was reported [170].

Catalyst-free cycloadditon of azides with strain-promoted alkynes have been employed in synthesis of topological T- and H-shaped polymers [171] and multiarm star polymers [172] by employing ATRP-generated functional polymers.

Star polymers constituting polypeptide arms for pH-responsive supramolecular assembly [173] and conjugated poly(3-hexylthiophene) arms [174, 175] via CuAAC methodology have been reported.

Diels–Alder and hetero Diels–Alder-based click methodologies have found practice in design and synthesis of various star architectures. Star and multiarm star polymers via Diels–Alder-based tailoring of clickable polymers were investigated by Hizal and co-workers. In this sense, multiarm star block copolymers [22] and multiarm star polymers with peripheral dendritic arms employing DA reaction was reported. The strategy included the utilization of protected maleimide or anthracene functional ATRP initiators in building up of clickable polymers. The proper choice of chain transfer agent in RAFT polymerization would allow the installation of HDA-clickable electron deficient dithioester groups at chain ends which leads to efficient synthesis of multi-arm star block copolymers [176, 177].

Aldehyde-aminooxy click reaction has been recently employed in synthesis of various star topologies by Lu and co-workers [178–180]. This facile reaction serves as a good alternative to commonly employed click concepts since the reaction proceeds smoothly in standard thermal conditions, without needing any UV source or metal catalyst.

The strategies of star polymer synthesis have also been extended to double-click and triple-click approaches where combinations of CuAAC/Diels–Alder [181, 182], (Fig. 16)

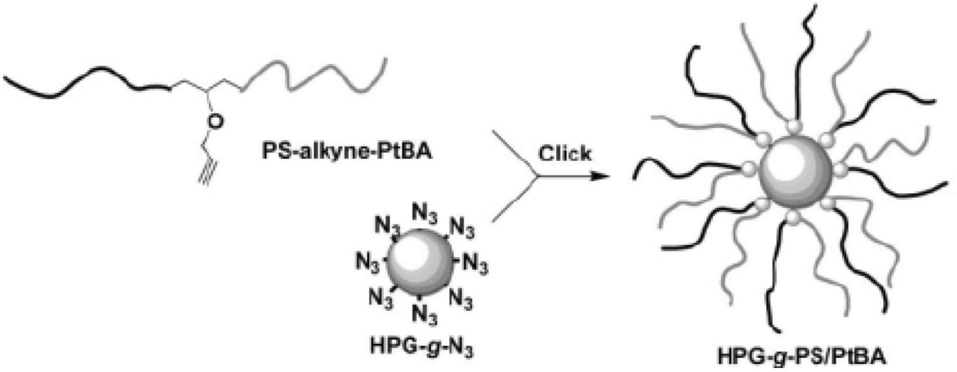


Fig. 14 Synthesis of hyperbranched polyglycerol core star polymers with ‘V’-shaped polymer arms. Adapted from [167] with permission. Copyright © 2008 by Wiley Periodicals, Inc

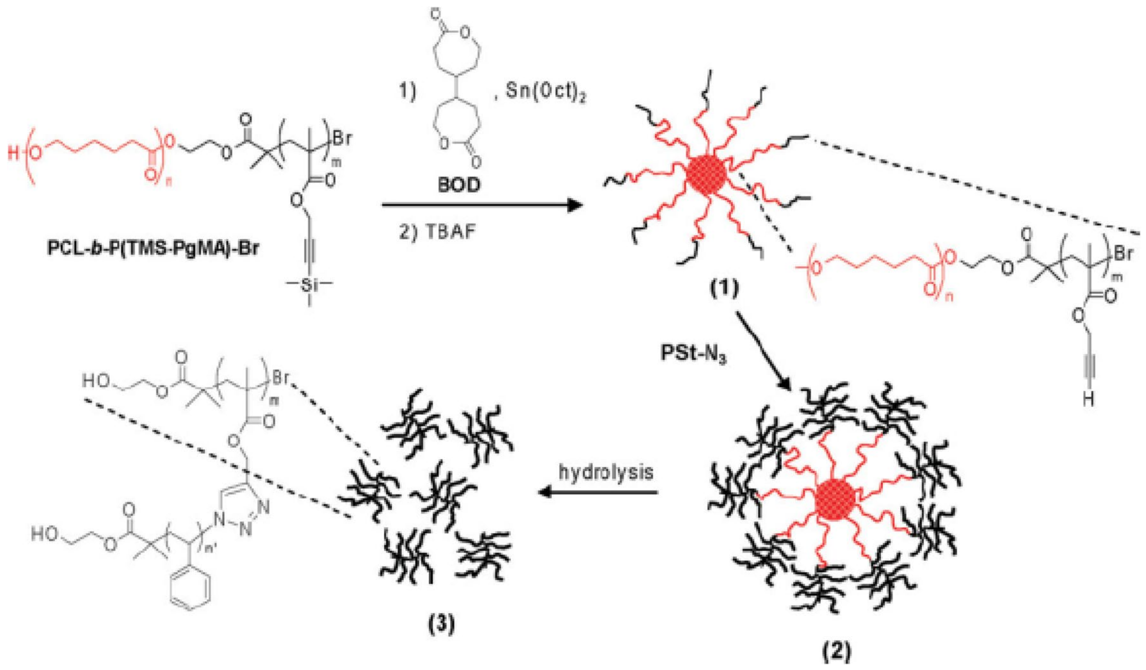


Fig. 15 Synthesis of core-crosslinked star block copolymers and subsequent hydrolysis to brush copolymers. From [169] with permission. Copyright © 2008 by Wiley Periodicals, Inc

CuAAC/thiol–ene [183], thiol–para–fluoro/thiol–ene [184] and CuAAC/Diels–Alder/thiol–ene [185] reactions were successfully employed in tailor-made architecturing.

2.5 Hyperbranched Polymers

Hyperbranched polymers own distinct structural morphologies in which majority of their physical characteristics, melt and solution behavior and interface properties could significantly differ from linear polymers. Application-wise fabrication of polymeric materials may require low melting temperatures and high fluidity, good solubility and low solution viscosities and presence of a large number of terminal functional groups. Highly branched molecular structures of hyperbranched polymers endue ample opportunities in various key applications such as, catalyst, energy storage, polymer processing and biomedical practice [186, 187].

The applications of click chemistry methodologies in synthesis of hyperbranched polymers follow mostly the conventional A_xB_y-type coupling of functional monomers. This strategy, combining with highly efficient click reactions leads to building up the macromolecular structure in a defect-free manner with well-controlled architecture and narrow size distributions.

The examples of CuAAC click reaction in fabrication of hyperbranched polymers include self-polymerization of a polystyrene-based AB_2 macromonomer including an azide group at its one end and two terminal propargyl functionalities at the other chain end [188]. CuAAC click reaction was demonstrated as a highly reactive and efficient tool to obtain unimodal molecular weight distribution of final complex structure. In case of click-propagating chain growing of two different functional blocks, multiblock hyperbranched copolymers could be achieved (Fig. 17) [189].

An interesting seesaw-type polystyrene macromonomer having a chain-centered alkynyl group and two azide groups at each chain ends was employed in defect-free synthesis of hyperbranched polymers with uniform sub-chains [190]. In a similar macromonomer design with self-assembly mediated CuAAC click reaction, janus long-chain hyperbranched copolymers with polystyrene and poly[oligo(ethylene glycol) methacrylate half-dendrons were successfully obtained [191].

Post-polymerization attachment of clickable polymers onto previously-constructed hyperbranched polymers with complementary clickable groups is another strategy to reach segmented hyperbranched polymers [192] [193]. This is a straightforward engineering of complex polymers with hydrophobic, hydrophilic or amphiphilic modifications to impart key features.

Thiol–yne click reaction-based synthesis of hyperbranched polymers has been investigated by Perrier and co-workers. This highly efficient click reaction allows buildup of branched polymers from thiol or alkyne functional small molecules or macromolecules [194]. In thiol-X

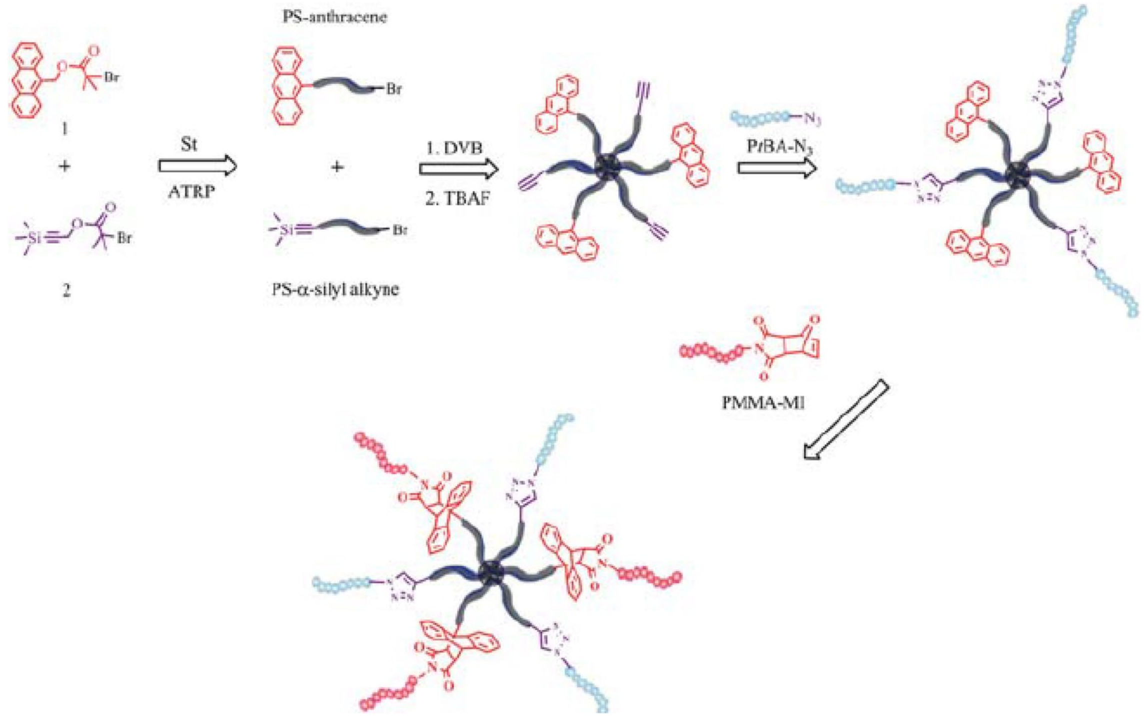


Fig. 16 Synthesis of multi-miktoarm star block copolymers via CuAAC/DA double-click strategy. From [181] with permission. Copyright © 2010 by The Royal Society of Chemistry

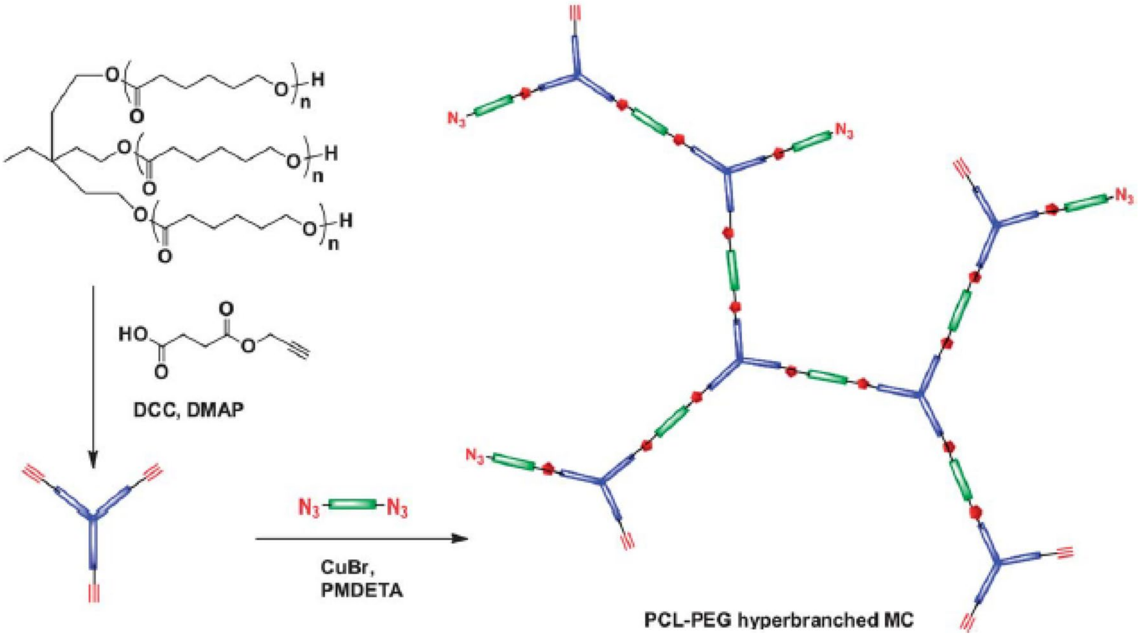


Fig. 17 CuAAC-mediated synthesis of multiblock hyperbranched copolymers with poly(e-caprolactone) and polyethylene glycol blocks. From [189] with permission. Copyright © 2013 by The Royal Society of Chemistry

based approaches, RAFT polymers have been utilized as good macromolecular thiol sources since the present thiocarbonyl groups at chain ends can be converted into thiols via various reduction techniques [195]. In case employing alkyne functional chain transfer agents and subsequent post-polymerization thiocarbonyl reduction, heterotelechelics with thiol–yne clickable end groups have been obtained and utilized towards hyperbranching [196, 197]. The peripheral/focal thiol or alkyne groups also serve as reactive handles for post-polymerization functionalization to attach various small molecules [198] and macromolecules [199]. In addition to this RAFT polymer-based architecturing, complementary alkyne and thiol groups can be installed on polymer ends via sequential post-polymerization modification [200].

3 Conclusion

Complex macromolecules endue some of unique molecular structures that impart key attributes in various applications. Regardless of employing small organic molecules or large polymers chains as building blocks towards the fabrication of discrete macromolecular constructs, synthetic methodologies hold key importance in successful implementation. Highly efficient, orthogonal and robust click reactions possess ample opportunities in synthesis of complex macromolecules especially when they combined with various polymerization methods and post-polymerization modification techniques. Click chemistry reactions operate in different reaction conditions (i.e. catalyst-aided or catalyst-free reaction coordinates thermal or UV activations, reversible reaction mechanisms) in which this diversity could be beneficial while implementing the optimum material design and synthesis.

References

1. Hadjichristidis N, Pitsikalis M, Pispas S, Iatrou H (2001) Polymers with complex architecture by living anionic polymerization. Chem Rev 101:3747–3792
2. Fournier D, Hoogenboom R, Schubert US (2007) Clicking polymers: a straightforward approach to novel macromolecular architectures. Chem Soc Rev 36:1369–1380
3. Tasdelen MA, Kiskan B, Yagci Y (2016) Externally stimulated click reactions for macromolecular syntheses. Prog Polym Sci 52:19–78
4. Kolb HC, Finn MG, Sharpless KB (2001) Click chemistry: diverse chemical function from a few good reactions. Angew Chem Int Ed 40:2004–2021
5. Meldal M (2008) Polymer "clicking" by CuAAC reactions. Macromol Rapid Commun 29:1016–1051
6. Binder WH, Sachsenhofer R (2008) "Click" chemistry in polymer and material science: an update. Macromol Rapid Commun 29:952–981
7. Such GK, Johnston APR, Liang K, Caruso F (2012) Synthesis and functionalization of nanoengineered materials using click chemistry. Prog Polym Sci 37:985–1003
8. Barner-Kowollik C, Inglis AJ (2009) Has click chemistry lead to a paradigm shift in polymer material design? Macromol Chem Phys 210:987–992
9. Li HK, Sun JZ, Qin AJ, Tang BZ (2012) Azide-alkyne click polymerization: an update. Chin J Polym Sci Engl Ed 30:1–15
10. Arslan M, Gok O, Sanyal R, Sanyal A (2014) Clickable poly(ethylene glycol)-based copolymers using azide-alkyne click cycloaddition-mediated step-growth polymerization. Macromol Chem Phys 215:2237–2247
11. Billiet L, Fournier D, Du Prez F (2009) Step-growth polymerization and "click" chemistry: the oldest polymers rejuvenated. Polymer 50:3877–3886
12. Tasdelen MA, Yagci Y (2010) Light-induced copper (I)-catalyzed click chemistry. Tetrahedron Lett 51:6945–6947
13. Tasdelen MA (2011) Poly(epsilon-caprolactone)/clay nanocomposites via "click" chemistry. Eur Polym J 47:937–941
14. Altin H, Kosif I, Sanyal R (2010) Fabrication of "clickable" hydrogels via dendron-polymer conjugates. Macromolecules 43:3801–3808
15. Arslan M, Tasdelen MA (2017) Polymer nanocomposites via click chemistry reactions. Polymers (Basel) 9:499
16. Acar SB, Ozcelik M, Uyar T, Tasdelen MA (2017) Polyhedral oligomeric silsesquioxane-based hybrid networks obtained via thiol-epoxy click chemistry. Iran Polym J 26:405–411
17. Li Y, Dong X-H, Zou Y, Wang Z, Yue K, Huang M, Liu H, Feng X, Lin Z, Zhang W (2017) Polyhedral oligomeric silsesquioxane meets "click" chemistry: rational design and facile preparation of functional hybrid materials. Polymer 125:303–329
18. Tasdelen MA (2011) Diels–Alder "click" reactions: recent applications in polymer and material science. Polym Chem 2:2133–2145
19. Hizal G, Tunca U, Sanyal A (2011) Discrete macromolecular constructs via the Diels–Alder "click" reaction. J Polym Sci Part A Polym Chem 49:4103–4120
20. Agar S, Durmaz H, Gunay US, Hizal G, Tunca U (2015) Polymer grafting onto polyurethane backbone via Diels–Alder reaction. J Polym Sci Part A Polym Chem 53:521–527
21. Durmaz H, Colakoglu B, Tunca U, Hizal G (2006) Preparation of block copolymers via Diels–Alder reaction of maleimide- and anthracene-end functionalized polymers. J Polym Sci Part A Polym Chem 44:1667–1675
22. Dag A, Durmaz H, Tunca U, Hizal G (2009) Multiarm star block copolymers via Diels–Alder click reaction. J Polym Sci Part A Polym Chem 47:178–187
23. Altinbasak I, Sanyal R, Sanyal A (2016) Best of both worlds: Diels–Alder chemistry towards fabrication of redox-responsive degradable hydrogels for protein release. RSC Adv 6:74757–74764
24. Gacal B, Durmaz H, Tasdelen MA, Hizal G, Tunca U, Yagci Y, Demirel AL (2006) Anthracene-maleimide-based Diels–Alder "click chemistry" as a novel route to graft copolymers. Macromolecules 39:5330–5336
25. Durmaz H, Dag A, Cerit N, Sirkecioglu O, Hizal G, Tunca U (2010) Graft copolymers via ROMP and Diels–Alder click reaction strategy. J Polym Sci Part A Polym Chem 48:5982–5991
26. Wang ZP, Yuan JY (2012) Applications of Diels–Alder reaction in synthesis of polymers with well-defined architectures. Prog Chem 24:2342–2351
27. Kose MM, Yesilbag G, Sanyal A (2008) Segment block dendrimers via Diels–Alder cycloaddition. Org Lett 10:2353–2356
28. Tonga M, Cengiz N, Merve Kose M, Dede T, Sanyal A (2010) Dendronized polymers via Diels–Alder "click" reaction. J Polym Sci Part A Polym Chem 48:410–416
29. Kalaoglu-Altan OI, Kirac-Aydin A, Sumer Bolu B, Sanyal R, Sanyal A (2017) Diels–Alder "clickable" biodegradable nanofibers: benign tailoring of scaffolds for biomolecular immobilization and cell growth. Bioconjug Chem 28:2420–2428
30. Arslan M (2018) The aqueous barbier polycondensation of biomass-derived 5-chloromethylfurfural: a proof of concept study to access functional polymers. Macromol Chem Phys 219:1800087

31. Xu Z, Bratlie KM (2018) Click chemistry and material selection for in situ fabrication of hydrogels in tissue engineering applications. ACS Biomater Sci Eng 4:2276–2291
32. Arslan M, Aydin D, Degirmenci A, Sanyal A, Sanyal R (2017) Embedding well-defined responsive hydrogels with nanocontainers: tunable materials from telechelic polymers and cyclodextrins. ACS Omega 2:6658–6667
33. Oz Y, Arslan M, Gevrek TN, Sanyal R, Sanyal A (2016) Modular fabrication of polymer brush coated magnetic nanoparticles: engineering the interface for targeted cellular imaging. ACS Appl Mater Interfaces 8:19813–19826
34. Arslan M, Gevrek TN, Sanyal R, Sanyal A (2015) Fabrication of poly(ethylene glycol)-based cyclodextrin containing hydrogels via thiol-ene click reaction. Eur Polym J 62:426–434
35. Arslan M, Gevrek TN, Sanyal A, Sanyal R (2014) Cyclodextrin mediated polymer coupling via thiol-maleimide conjugation: facile access to functionalizable hydrogels. RSC Adv 4:57834–57841
36. Arslan M, Gevrek TN, Lyskawa J, Szunerits S, Boukherroub R, Sanyal R, Woisel P, Sanyal A (2014) Bioinspired anchorable thiol-reactive polymers: synthesis and applications toward surface functionalization of magnetic nanoparticles. Macromolecules 47:5124–5134
37. Yilmaz II, Arslan M, Sanyal A (2012) Design and synthesis of novel “orthogonally” functionalizable maleimide-based styrenic copolymers. Macromol Rapid Commun 33:856–862
38. Yang Z, Chen Q, Zhou D, Bu Y (2012) Synthesis of functional polymer materials via thiol-ene/yne click chemistry. Prog Chem 24:395–404
39. Uygun M, Tasdelen MA, Yagci Y (2010) Influence of type of initiation on thiol–ene “click” chemistry. Macromol Chem Phys 211:103–110
40. Agar S, Baysak E, Hizal G, Tunca U, Durmaz H (2018) An emerging post-polymerization modification technique: the promise of thiol-para-fluoro click reaction. J Polym Sci Part A: Polym Chem 56:1181–1198
41. Kakuchi R (2014) Multicomponent reactions in polymer synthesis. Angew Chem Int Ed 53:46–48
42. Tunca U (2018) Click and multicomponent reactions work together for polymer chemistry. Macromol Chem Phys 219:1800163
43. Abdul Fattah T, Saeed A, Albericio F (2018) Recent advances towards sulfur(VI) fluoride exchange (SuFEx) click chemistry. J Fluor Chem 213:87–112
44. Shi Y, Sun JZ, Qin A (2017) Click polymerization: the aurora of polymer synthetic methodology. J Polym Sci Part A Polym Chem 55:616–621
45. Zou Y, Zhang L, Yang L, Zhu F, Ding M, Lin F, Wang Z, Li Y (2018) “Click” chemistry in polymeric scaffolds: bioactive materials for tissue engineering. J Control Release 273:160–179
46. Martens S, Holloway JO, Du Prez FE (2017) Click and click-inspired chemistry for the design of sequence-controlled polymers. Macromol Rapid Commun 38:1700469
47. Escorihuela J, Marcelis ATM, Zuilhof H (2015) Metal-free click chemistry reactions on surfaces. Adv Mater Interfaces 2:1500135
48. Denkova AG, Mendes E, Coppens MO (2010) Non-equilibrium dynamics of block copolymer micelles in solution: recent insights and open questions. Soft Mater 6:2351–2357
49. Jain S, Bates FS (2003) On the origins of morphological complexity in block copolymer surfactants. Science 300:460–464
50. Mai Y, Eisenberg A (2012) Self-assembly of block copolymers. Chem Soc Rev 41:5969–5985
51. Li F, Xie C, Cheng Z, Xia H (2016) Ultrasound responsive block copolymer micelle of poly(ethylene glycol)-poly(propylene glycol) obtained through click reaction. Ultrason Sonochem 30:9–17
52. Yuan W, Zhang J, Wei J (2011) Synthesis of well-defined polymer via a combination of click chemistry and living radical polymerization. Prog Chem 23:760–771
53. Akeroyd N, Klumperman B (2011) The combination of living radical polymerization and click chemistry for the synthesis of advanced macromolecular architectures. Eur Polym J 47:1207–1231
54. Tasdelen MA, Kahveci MU, Yagci Y (2011) Telechelic polymers by living and controlled/living polymerization methods. Prog Polym Sci 36:455–567
55. Gregory A, Stenzel MH (2012) Complex polymer architectures via RAFT polymerization: from fundamental process to extending the scope using click chemistry and nature’s building blocks. Prog Polym Sci 37:38–105
56. Quémener D, Davis TP, Barner-Kowollik C, Stenzel MH (2006) RAFT and click chemistry: a versatile approach to well-defined block copolymers. Chem Commun 48:5051–5053
57. Liu X, Feng X, Chen J, Cao Y (2013) Synthesis of block copolymers based on *N*-alkyl substituted acrylamide via combination of reversible addition-fragmentation transfer polymerization and click chemistry. J Macromol Sci Part A Pure Appl Chem 50:65–71
58. Opsteen JA, Van Hest JCM (2007) Modular synthesis of ABC type block copolymers by “click” chemistry. J Polym Sci Part A Polym Chem 45:2913–2924
59. Berges C, Javakhishvili I, Hvilsted S, Sánchez C, Alcalá R (2012) Photoresponsive azopolyester-PMMA block copolymers obtained by combination of ATRP, polycondensation, and “click” chemistry. Macromol Chem Phys 213:2299–2310
60. Agut W, Taton D, Lecommandoux S (2007) A versatile synthetic approach to polypeptide based rod-coil block copolymers by click chemistry. Macromolecules 40:5653–5661
61. Okcu SS, Durmaz YY, Yagci Y (2010) Synthesis and characterization of telechelic block co-polymers by combination of atom transfer radical polymerization and click chemistry processes. Des Monomers Polym 13:459–472
62. Capacchione C, De Roma A, Buonerba A, Speranza V, Milione S, Grassi A (2013) Syndiotactic polystyrene-block-poly(methyl methacrylate) copolymer via click chemistry. Macromol Chem Phys 214:1990–1997
63. Coessens V, Matyjaszewski K (1999) End group transformation of polymers prepared by ATRP, substitution to azides. J Macromol Sci Pure Appl Chem A 36:667–679
64. Golas PL, Tsarevsky NV, Sumerlin BS, Walker LM, Matyjaszewski K (2007) Multisegmented block copolymers by click coupling of polymers prepared by ATRP. Aust J Chem 60:400–404
65. He X, Liang L, Wang K, Lin S, Yan D, Zhang Y (2009) A new synthetic approach to asymmetric amphiphilic ABA′ block copolymers by ATRP and click reactions. J Appl Polym Sci 111:560–565
66. Patel VK, Vishwakarma NK, Mishra AK, Biswas CS, Maiti P, Ray B (2013) Synthesis of alkyne-terminated xanthate RAFT agents and their uses for the controlled radical polymerization of *N*-vinylpyrrolidone and the synthesis of its block copolymer using click chemistry. J Appl Polym Sci 127:4305–4317
67. Guerre M, Semsarilar M, Totée C, Silly G, Améduri B, Ladmiral V (2017) Self-assembly of poly(vinylidene fluoride)-: block -poly(2-(dimethylamino)ethylmethacrylate) block copolymers prepared by CuAAC click coupling. Polym Chem 8:5203–5211
68. Nasrullah MJ, Vora A, Webster DC (2011) Block copolymer synthesis via a combination of ATRP and RAFT using click chemistry. Macromol Chem Phys 212:539–549
69. Yang X, Van Duren JKJ, Janssen RAJ, Michels MAJ, Loos J (2004) Morphology and thermal stability of the active layer in poly(p-phenylenevinylene)/methanofullerene plastic photovoltaic devices. Macromolecules 37:2151–2158

70. Urien M, Erothu H, Cloutet E, Hiorns RC, Vignau L, Cramail H (2008) Poly(3-hexylthiophene) based block copolymers prepared by "click" chemistry. Macromolecules 41:7033–7040
71. Kempf CN, Smith KA, Pesek SL, Li X, Verduzco R (2013) Amphiphilic poly(alkylthiophene) block copolymers prepared via externally initiated GRIM and click coupling. Polym Chem 4:2158–2163
72. Smith KA, Pickel DL, Yager K, Kisslinger K, Verduzco R (2014) Conjugated block copolymers via functionalized initiators and click chemistry. J Polym Sci Part A Polym Chem 52:154–163
73. Pressly ED, Amir RJ, Hawker CJ (2011) Rapid synthesis of block and cyclic copolymers via click chemistry in the presence of copper nanoparticles. J Polym Sci Part A: Polym Chem 49:814–819
74. Fleischmann S, Komber H, Appelhans D, Voit BI (2007) Synthesis of functionalized NMP initiators for click chemistry: a versatile method for the preparation of functionalized polymers and block copolymers. Macromol Chem Phys 208:1050–1060
75. Touris A, Hadjichristidis N (2011) Cyclic and multiblock polystyrene-block-polyisoprene copolymers by combining anionic polymerization and azide/alkyne "click" chemistry. Macromolecules 44:1969–1976
76. Zhang M, Rupar PA, Feng C, Lin K, Lunn DJ, Oliver A, Nunns A, Whittell GR, Manners I, Winnik MA (2013) Modular synthesis of polyferrocenylsilane block copolymers by Cu-catalyzed alkyne/azide "click" reactions. Macromolecules 46:1296–1304
77. Reuther JF, Siriwardane DA, Kulikov OV, Batchelor BL, Campos R, Novak BM (2015) Facile synthesis of rod-coil block copolymers with chiral, helical polycarbodiimide segments via postpolymerization CuAAC "click" coupling of functional end groups. Macromolecules 48:3207–3216
78. Gulyuz S, Ozkose UU, Kocak P, Telci D, Yilmaz O, Tasdelen MA (2018) In-vitro cytotoxic activities of poly(2-ethyl-2-oxazoline)-based amphiphilic block copolymers prepared by CuAAC click chemistry. Express Polym Lett 12:146–158
79. Zhou QH, Zheng JK, Shen Z, Fan XH, Chen XF, Zhou QF (2010) Synthesis and hierarchical self-assembly of rod-rod block copolymers via click chemistry between mesogen-jacketed liquid crystalline polymers and helical polypeptides. Macromolecules 43:5637–5646
80. Glaied O, Delaite C, Riess G (2012) Synthesis of PCL-b-PVAc block copolymers by combination of click chemistry, ROP, and RAFT polymerizations. Polym Bull 68:607–621
81. Oyman Eyrilmez G, Doran S, Murtezi E, Demir B, Odaci Demirkol D, Coskunol H, Timur S, Yagci Y (2015) Selective cell adhesion and biosensing applications of bio-active block copolymers prepared by CuAAC/thiol-ene double click reactions. Macromol Biosci 15:1233–1241
82. Wu Q, Yi J, Wang S, Liu D, Song X, Zhang G (2015) Synthesis and self-assembly of new amphiphilic thermosensitive poly(*N*-vinylcaprolactam)/poly(d, l-lactide) block copolymers via the combination of ring-opening polymerization and click chemistry. Polym Bull 72:1449–1466
83. Pal A, Pal S (2017) Synthesis of poly (ethylene glycol)-block-poly (acrylamide)-block-poly (lactide) amphiphilic copolymer through ATRP, ROP and click chemistry: characterization, micellization and pH-triggered sustained release behaviour. Polymer 127:150–158
84. Tirino P, Conte C, Ordegno M, Palumbo R, Ungaro F, Quaglia F, Maglio G (2014) Y- and H-shaped amphiphilic PEG-pcl block copolymers synthesized combining ring-opening polymerization and click chemistry: characterization and self-assembly behavior. Macromol Chem Phys 215:1218–1229
85. Luo Y, Montarnal D, Treat NJ, Hustad PD, Christianson MD, Kramer EJ, Fredrickson GH, Hawker CJ (2015) Enhanced block copolymer phase separation using click chemistry and ionic junctions. ACS Macro Lett 4:1332–1336
86. Hilf S, Hanik N, Kilbinger AFM (2008) A "click" approach to ROMP block copolymers. J Polym Sci Part A Polym Chem 46:2913–2921
87. Hua C, Dong CM, Wei Y (2009) Versatile strategy for the synthesis of dendronlike polypeptide/linear poly(ε-caprolactone) block copolymers via click chemistry. Biomacromolecules 10:1140–1148
88. Blasco E, Del Barrio J, Piñol M, Oriol L, Berges C, Sánchez C, Alcalá R (2012) Azobenzene-containing linear-dendritic block copolymers prepared by sequential ATRP and click chemistry. Polymer 53:4604–4613
89. Del Barrio J, Oriol L, Alcalá R, Sánchez C (2010) Photoresponsive poly(methyl methacrylate)-b-azodendron block copolymers prepared by ATRP and click chemistry. J Polym Sci Part A Polym Chem 48:1538–1550
90. Durmaz H, Sanyal A, Hizal G, Tunca U (2012) Double click reaction strategies for polymer conjugation and post-functionalization of polymers. Polym Chem 3:825–835
91. Omurtag PS, Gunay US, Dag A, Durmaz H, Hizal G, Tunca U (2013) Diels–Alder click reaction for the preparation of polycarbonate block copolymers. J Polym Sci Part A Polym Chem 51:2252–2259
92. Hsu YI, Masutani K, Yamaoka T, Kimura Y (2015) Strengthening of hydrogels made from enantiomeric block copolymers of polylactide (PLA) and poly(ethylene glycol) (PEG) by the chain extending Diels–Alder reaction at the hydrophilic PEG terminals. Polymer 67:157–166
93. Gok O, Yigit S, Merve Kose M, Sanyal R, Sanyal A (2013) Dendron-polymer conjugates via the Diels–Alder "click" reaction of novel anthracene-based dendrons. J Polym Sci Part A Polym Chem 51:3191–3201
94. Kempe K, Onbulak S, Schubert US, Sanyal A, Hoogenboom R (2013) PH degradable dendron-functionalized poly(2-ethyl-2-oxazoline) prepared by a cascade "double-click" reaction. Polym Chem 4:3236–3244
95. Sinnwell S, Inglis AJ, Davis TP, Stenzel MH, Barner-Kowollik C (2008) An atom-efficient conjugation approach to well-defined block copolymers using RAFT chemistry and hetero Diels-Alder cycloaddition. Chem Commun 17:2052–2054
96. Inglis AJ, Stenzel MH, Barner-Kowollik C (2009) Ultra-fast raft-hda click conjugation: an efficient route to high molecular weight block copolymersa. Macromol Rapid Commun 30:1792–1798
97. Espinosa E, Glassner M, Boisson C, Barner-Kowollik C, D'Agosto F (2011) Synthesis of cyclopentadienyl capped polyethylene and subsequent block copolymer formation via hetero diels-alder (HDA) chemistry. Macromol Rapid Commun 32:1447–1453
98. Langer M, Brandt J, Lederer A, Goldmann AS, Schacher FH, Barner-Kowollik C (2014) Amphiphilic block copolymers featuring a reversible hetero Diels–Alder linkage. Polym Chem 5:5330–5338
99. Sprafke JK, Spruell JM, Mattson KM, Montarnal D, McGrath AJ, Pötzsch R, Miyajima D, Hu J, Latimer AA, Voit BI, Aida T, Hawker CJ (2015) Revisiting thiol–yne chemistry: selective and efficient monoaddition for block and graft copolymer formation. J Polym Sci Part A Polym Chem 53:319–326
100. Barner-Kowollik C, Du Prez FE, Espeel P, Hawker CJ, Junkers T, Schlaad H, Van Camp W (2011) "Clicking" polymers or just efficient linking: what is the difference? Angew Chem Int Ed 50:60–62
101. Novoa-Carballal R, Müller AHE (2012) Synthesis of polysaccharide-b-PEG block copolymers by oxime click. Chem Commun 48:3781–3783
102. Novoa-Carballal R, Silva C, Möller S, Schnabelrauch M, Reis RL, Pashkuleva I (2014) Tunable nano-carriers from

clicked glycosaminoglycan block copolymers. J Mater Chem B 2:4177–4184

103. Yang B, Zhao Y, Fu C, Zhu C, Zhang Y, Wang S, Wei Y, Tao L (2014) Introducing the Ugi reaction into polymer chemistry as a green click reaction to prepare middle-functional block copolymers. Polym Chem 5:2704–2708
104. Tsutsuba T, Sogawa H, Takata T (2017) Preparation of a highly reactive polymer click reagent, PEG nitrile: n-oxide, and its application in block and star polymer synthesis. Polym Chem 8:1445–1448
105. Cai T, Neoh KG, Kang ET (2012) Surface-functionalized and surface-functionalizable poly(vinylidene fluoride) membranes via controlled/living radical polymerization and click chemistry. ACS Symp Ser 1101:211–229
106. Yin J, Ge Z, Liu H, Liu S (2009) Synthesis of amphiphilic copolymer brushes possessing alternating poly(methyl methacrylate) and poly(*N*-isopropylacrylamide) grafts via a combination of aTRp and click chemistry. J Polym Sci Part A Polym Chem 47:2608–2619
107. Tsarevsky NV, Bencherif SA, Matyjaszewski K (2007) Graft copolymers by a combination of ATRP and two different consecutive click reactions. Macromolecules 40:4439–4445
108. Quémener D, Le Hellaye M, Bissett C, Davis TP, Barner-Kowollik C, Stenzel MH (2008) Graft block copolymers of propargyl methacrylate and vinyl acetate via a combination of RAFT/MADIX and click chemistry: reaction analysis. J Polym Sci Part A Polym Chem 46:155–173
109. Pang X, Zhao L, Feng C, Wu R, Ma H, Lin Z (2013) Functional copolymer brushes composed of a hydrophobic backbone and densely grafted conjugated side chains via a combination of living polymerization with click chemistry. Polym Chem 4:2025–2032
110. Freichels H, Pourcelle V, Auzély-Velty R, Marchand-Brynaert J, Jérôme C (2012) Synthesis of poly(lactide-*co*-glycolide-*co*-ε-caprolactone)-graft- mannosylated poly(ethylene oxide) copolymers by combination of "clip" and "click" chemistries. Biomacromolecules 13:760–768
111. Zhang K, Wang Y, Zhu W, Li X, Shen Z (2012) Synthesis, characterization, and micellization of PCL-g-PEG copolymers by combination of ROP and "click" chemistry via "graft onto" method. J Polym Sci Part A Polym Chem 50:2045–2052
112. Li M, Pan P, Shan G, Bao Y (2015) Thermoresponsive poly(ε{lunate}-caprolactone)-graft-poly(*N*-isopropylacrylamide) graft copolymers prepared by a combination of ring-opening polymerization and sequential azide-alkyne click chemistry. Polym Int 64:389–396
113. Şanal T, Koçak İ, Hazer B (2017) Synthesis of comb-type amphiphilic graft copolymers derived from chlorinated poly(ε-caprolactone) via click reaction. Polym Bull 74:977–995
114. Zhang X, Zhang Z, Zhong Z, Zhuo R (2012) Amphiphilic block-graft copolymers poly(ethylene glycol)-b-(polycarbonates-g-palmitate) prepared via the combination of ring-opening polymerization and click chemistry. J Polym Sci Part A Polym Chem 50:2687–2696
115. Lav TX, Lemechko P, Renard E, Amiel C, Langlois V, Volet G (2013) Development of a new azido-oxazoline monomer for the preparation of amphiphilic graft copolymers by combination of cationic ring-opening polymerization and click chemistry. React Funct Polym 73:1001–1008
116. Eissa AM, Khosravi E (2015) Comb-like graft copolymers of poly(oxa)norbornene: efficient synthesis using a combination of ROMP and click chemistry. Macromol Chem Phys 216:964–976
117. Enomoto-Rogers Y, Kamitakahara H, Yoshinaga A, Takano T (2012) Comb-shaped graft copolymers with cellulose side-chains prepared via click chemistry. Carbohydr Polym 87:2237–2245
118. Tizzotti M, Creuzet C, Labeau MP, Hamaide T, Boisson F, Drockenmuller E, Charlot A, Fleury E (2010) Synthesis of temperature responsive biohybrid guar-based grafted copolymers by click chemistry. Macromolecules 43:6843–6852
119. Bertoldo M, Zampano G, La Terra F, Villari V, Castelvetro V (2011) Amphiphilic amylose-g-poly(meth)acrylate copolymers through "click" onto grafting method. Biomacromolecules 12:388–398
120. Borsacchi S, Calucci L, Geppi M, La Terra F, Pinzino C, Bertoldo M (2014) Characterization of an amylose-graft-poly(n-butyl methacrylate) copolymer obtained by click chemistry by EPR and SS-NMR spectroscopies. Carbohydr Polym 112:245–254
121. Yuan WZ, Zhao ZD, Gu SY, Ren TB, Ren J (2011) Synthesis and self-assembly of pH-responsive chitosan graft copolymer by the combination of atom transfer radical polymerization and click chemistry. Mater Lett 65:793–796
122. Enomoto-Rogers Y, Iwata T (2012) Synthesis of xylan-graft-poly(L-lactide) copolymers via click chemistry and their thermal properties. Carbohydr Polym 87:1933–1940
123. Li Q, Kang H, Liu R, Huang Y (2012) Block and hetero ethyl cellulose graft copolymers synthesized via sequent and one-pot ATRP and "click" reactions. Chin J Chem 30:2169–2175
124. Lemechko P, Renard E, Guezennec J, Simon-Colin C, Langlois V (2012) Synthesis of dextran-graft-PHBHV amphiphilic copolymer using click chemistry approach. React Funct Polym 72:487–494
125. Feng C, Li Y, Yang D, Hu J, Zhang X, Huang X (2011) Well-defined graft copolymers: from controlled synthesis to multipurpose applications. Chem Soc Rev 40:1282–1295
126. Demirci G, Tasdelen MA (2015) Synthesis and characterization of graft copolymers by photoinduced CuAAC click chemistry. Eur Polym J 66:282–289
127. Acik G, Sey E, Tasdelen MA (2018) Polypropylene-based graft copolymers via CuAAC click chemistry. Express Polym Lett 12:418–428
128. Lee KW, Chung JW, Kwak SY (2016) Structurally enhanced self-plasticization of poly(vinyl chloride) via click grafting of hyperbranched polyglycerol. Macromol Rapid Commun 37:2045–2051
129. Obhi NK, Peda DM, Kynaston EL, Seferos DS (2018) Exploring the graft-to synthesis of all-conjugated comb copolymers using azide-alkyne click chemistry. Macromolecules 51:2969–2978
130. Lin W, Fu Q, Zhang Y, Huang J (2008) One-pot synthesis of ABC type triblock copolymers via a combination of "click chemistry" and atom transfer nitroxide radical coupling chemistry. Macromolecules 41:4127–4135
131. Naolou T, Busse K, Kressler J (2010) Synthesis of well-defined graft copolymers by combination of enzymatic polycondensation and "Click" chemistry. Biomacromolecules 11:3660–3667
132. Yilmaz G, Toiserkani H, Demirkol DO, Sakarya S, Timur S, Torun L, Yagci Y (2011) Polysulfone based amphiphilic graft copolymers by click chemistry as bioinert membranes. Mater Sci Eng C 31:1091–1097
133. Yilmaz G, Toiserkani H, Demirkol DO, Sakarya S, Timur S, Yagci Y, Torun L (2011) Modification of polysulfones by click chemistry: amphiphilic graft copolymers and their protein adsorption and cell adhesion properties. J Polym Sci Part A Polym Chem 49:110–117
134. Agar S, Durmaz H, Gunay US, Hizal G, Tunca U (2014) Polymer grafting onto polyurethane backbone via Diels–Alder reaction. J Polym Sci Part A Polym Chem 53:521–527
135. Dag A, Aydin M, Durmaz H, Hizal G, Tunca U (2012) Various polycarbonate graft copolymers via Diels–Alder click reaction. J Polym Sci Part A Polym Chem 50:4476–4483
136. Durmaz H, Dag A, Hizal G, Tunca U (2011) Sequential double polymer click reactions for the preparation of regular graft copolymers. J Polym Sci Part A Polym Chem 49:1195–1200

137. Dag A, Sahin H, Durmaz H, Hizal G, Tunca U (2011) Block-brush copolymers via ROMP and sequential double click reaction strategy. J Polym Sci Part A Polym Chem 49:886–892
138. Gunay US, Ozsoy B, Durmaz H, Hizal G, Tunca U (2013) V-shaped graft copolymers via triple click reactions: Diels–Alder, copper-catalyzed azide-alkyne cycloaddition, and nitroxide radical coupling. J Polym Sci Part A Polym Chem 51:4667–4674
139. Bousquet A, Barner-Kowollik C, Stenzel MH (2010) Synthesis of comb polymers via grafting-onto macromoleeules bearing pendant diene groups via the Hetero–Diels–Alder-raft click concept. J Polym Sci Part A Polym Chem 48:1773–1781
140. Abd Rabo Moustafa MM, Gillies ER (2013) Rubber functionalization by Diels–Alder chemistry: from cross-linking to multifunctional graft copolymer synthesis. Macromolecules 46:6024–6030
141. Tonga M, Yesilbag Tonga G, Seber G, Gok O, Sanyal A (2013) Dendronized polystyrene via orthogonal double-click reactions. J Polym Sci Part A Polym Chem 51:5029–5037
142. Le Fer G, Babinot J, Versace DL, Langlois V, Renard E (2012) An efficient thiol-ene chemistry for the preparation of amphiphilic PHA-based graft copolymers. Macromol Rapid Commun 33:2041–2045
143. Ott C, Hoogenboom R, Schubert US (2008) Post-modification of poly(pentafluorostyrene): a versatile "click" method to create well-defined multifunctional graft copolymers. Chem Commun 30:3516–3518
144. Jia Z, Monteiro MJ (2012) Cyclic polymers: methods and strategies. J Polym Sci Part A Polym Chem 50:2025–2097
145. Laurent BA, Grayson SM (2011) Synthesis of cyclic dendronized polymers via divergent "graft- from" and convergent click "graft-to" routes: preparation of modular toroidal macromolecules. J Am Chem Soc 133:13421–13429
146. Li M, Liu C, Hong CY, Pan CY (2015) Synthesis of graft copolymer with pendant macrocycles via combination of ATRP and click chemistry. Polymer 71:23–30
147. Josse T, De Winter J, Dubois P, Coulembier O, Gerbaux P, Memboeuf A (2015) A tandem mass spectrometry-based method to assess the architectural purity of synthetic polymers: a case of a cyclic polylactide obtained by click chemistry. Polym Chem 6:64–69
148. Sugai N, Heguri H, Ohta K, Meng Q, Yamamoto T, Tezuka Y (2010) Effective click construction of bridged-and spiro-multicyclic polymer topologies with tailored cyclic prepolymers (kyklo-telechelics). J Am Chem Soc 132:14790–14802
149. Fan X, Huang B, Wang G, Huang J (2012) Synthesis of amphiphilic heteroeight-shaped polymer cyclic -[poly(ethylene oxide)-b-polystyrene] 2 via "click" chemistry. Macromolecules 45:3779–3786
150. Huang Z, Zhou Y, Wang Z, Li Y, Zhang W, Zhou N, Zhang Z, Zhu X (2017) Recent advances of CuAAC click reaction in building cyclic polymer. Chin J Polym Sci Engl Ed 35:317–341
151. Qu L, Sun P, Wu Y, Zhang K, Liu Z (2017) Efficient homodifunctional bimolecular ring-closure method for cyclic polymers by combining RAFT and self-accelerating click reaction. Macromol Rapid Commun 38:1700121
152. Sun P, Chen J, Liu J, Zhang K (2017) Self-accelerating click reaction for cyclic polymer. Macromolecules 50:1463–1472
153. Li Z, Qu L, Zhu W, Liu J, Chen JQ, Sun P, Wu Y, Liu Z, Zhang K (2018) Self-accelerating click reaction for preparing cyclic polymers from unconjugated vinyl monomers. Polymer 137:54–62
154. Durmaz H, Dag A, Hizal G, Tunca U (2010) Cyclic homo and block copolymers through sequential double click reactions. J Polym Sci Part A Polym Chem 48:5083–5091
155. Glassner M, Blinco JP, Barner-Kowollik C (2011) Diels–Alder reactions as an efficient route to high purity cyclic polymers. Macromol Rapid Commun 32:724–728
156. Lu D, Jia Z, Monteiro MJ (2013) Synthesis of alkyne functional cyclic polymers by one-pot thiol-ene cyclization. Polym Chem 4:2080–2089
157. Ren JM, McKenzie TG, Fu Q, Wong EHH, Xu J, An Z, Shanmugam S, Davis TP, Boyer C, Qiao GG (2016) Star polymers. Chem Rev 116:6743–6836
158. Inoue K (2000) Functional dendrimers, hyperbranched and star polymers. Prog Polym Sci 25:453–571
159. Kempe K, Krieg A, Becer CR, Schubert US (2012) "Clicking" on/with polymers: a rapidly expanding field for the straightforward preparation of novel macromolecular architectures. Chem Soc Rev 41:176–191
160. Whittaker MR, Urbani CN, Monteiro MJ (2006) Synthesis of 3-miktoarm stars and 1st generation mikto dendritic copolymers by "living" radical polymerization and "click" chemistry. J Am Chem Soc 128:11360–11361
161. Gou PF, Zhu WP, Zhu N, Shen ZQ (2009) Synthesis and characterization of novel resorcinarene- centered amphiphilic star-block copolymers consisting of eight ABA triblock arms by combination of ROP, ATRP, and click chemistry. J Polym Sci Part A Polym Chem 47:2905–2916
162. Vora A, Singh K, Webster DC (2009) A new approach to 3-miktoarm star polymers using a combination of reversible addition-fragmentation chain transfer (RAFT) and ring opening polymerization (ROP) via "Click" chemistry. Polymer 50:2768–2774
163. Glauser T, Stancik CM, Möller M, Voytek S, Gast AP, Hedrick JL (2002) Dendritic-linear miktoarm star polymers from orthogonal protected initiators. Macromolecules 35:5774–5781
164. Yang LP, Dong XH, Pan CY (2008) Synthesis of inverse star block copolymer by combination of ATRP, ring opening polymerization, and "click chemistry". J Polym Sci Part A Polym Chem 46:7757–7772
165. Yang L, Zhou H, Shi G, Wang Y, Pan CY (2008) Synthesis of ABCD 4-miktoarm star polymers by combination of RAFT, ROP, and "click chemistry". J Polym Sci Part A Polym Chem 46:6641–6653
166. Gao H, Min K, Matyjaszewski K (2007) Synthesis of 3-arm star block copolymers by combination of "core-first" and "coupling-onto" methods using ATRP and click reactions. Macromol Chem Phys 208:1370–1378
167. Wang G, Liu C, Pan M, Huang J (2009) Synthesis and characterization of star graft copolymers with asymmetric mixed "v-shaped" side chains via "click" chemistry on a hyperbranched polyglycerol core. J Polym Sci Part A Polym Chem 47:1308–1316
168. Ten Brummelhuis N, Schlaad H (2011) Stimuli-responsive star polymers through thiol-yne core functionalization/crosslinking of block copolymer micelles. Polym Chem 2:1180–1184
169. Wiltshire JT, Qiao GC (2009) Degradable star polymers with high "click" functionality. J Polym Sci Part A Polym Chem 47:1485–1498
170. Durmaz H, Dag A, Erdogan E, Demirel AL, Hizal G, Tunca U (2010) Multiarm star block and multiarm star mixed-block copolymers via azide-alkyne click reaction. J Polym Sci Part A Polym Chem 48:99–108
171. Zhu W, Li Z, Sun P, Ren L, Zhang K (2016) T-shaped and H-shaped polymers constructed from UV-induced strain promoted azide-alkyne cycloaddition reaction. Polymer 86:1–7
172. Wang S, Yang X, Zhu W, Zou L, Zhang K, Chen Y, Xi F (2014) Strain-promoted azide-alkyne cycloaddition "click" as a conjugation tool for building topological polymers. Polymer 55:4812–4819

173. Rao J, Zhang Y, Zhang J, Liu S (2008) Facile preparation of well-defined AB > 2Y-shaped miktoarm star polypeptide copolymer via the combination of ring-opening polymerization and click chemistry. Biomacromolecules 9:2586–2593
174. Park J, Moon HC, Kim JK (2013) Facile synthesis for well-defined A2B miktoarm star copolymer of poly(3-hexylthiophene) and poly(methyl methacrylate) by the combination of anionic polymerization and click reaction. J Polym Sci Part A Polym Chem 51:2225–2232
175. Han D, Tong X, Zhao Y (2012) Synthesis and characterization of six-arm star polystyrene-block-poly (3-hexylthiophene) copolymer by combination of atom transfer radical polymerization and click reaction. J Polym Sci Part A Polym Chem 50:4198–4205
176. Sinnwell S, Inglis AJ, Stenzel MH, Barner-Kowollik C (2008) Access to three-arm star block copolymers by a consecutive combination of the copper(I)-catalyzed azide-alkyne cycloaddition and the RAFT hetero Diels–Alder concept. Macromol Rapid Commun 29:1090–1096
177. Sinnwell S, Lammens M, Stenzel MH, Du Prez FE, Barner-Kowollik C (2009) Efficient access to multi-arm star block copolymers by a combination of ATRP and RAFT-HDA click chemistry. J Polym Sci Part A Polym Chem 47:2207–2213
178. Wu ZM, Liang H, Lu J, Deng WLI (2010) Miktoarm star copolymers via combination of RAFT arm-first technique and aldehyde-aminooxy click reaction. J Polym Sci Part A Polym Chem 48:3323–3330
179. Wu Z, Liang H, Lu J (2010) Synthesis of poly(*N*-isopropylacrylamide)-poly(ethylene glycol) miktoarm star copolymers via RAFT polymerization and aldehyde-aminooxy click reaction and their thermoinduced micellization. Macromolecules 43:5699–5705
180. Huang J, Xiao Z, Liang H, Lu J (2014) Star graft copolymer via grafting-onto strategy using a comb!ination of reversible addition–fragmentation chain transfer arm-first technique and aldehyde–aminooxy click reaction. Polym Int 63:1122–1128
181. Dag A, Durmaz H, Kirmizi V, Hizal G, Tunca U (2010) An easy way to the preparation of multi-miktoarm star block copolymers via sequential double click reactions. Polym Chem 1:621–623
182. Liu H, Pan W, Tong M, Zhao Y (2016) Synthesis and properties of couplable ABCDE star copolymers by orthogonal CuAAC and Diels–Alder click reactions. Polym Chem 7:1603–1611
183. Iskin B, Yilmaz G, Yagci Y (2011) ABC type miktoarm star copolymers through combination of controlled polymerization techniques with thiol-ene and azide-alkyne click reactions. J Polym Sci Part A Polym Chem 49:2417–2422
184. Cakir N, Tunca U, Hizal G, Durmaz H (2016) Heterofunctionalized multiarm star polymers via sequential thiol-para-fluoro and thiol-ene double “Click” reactions. Macromol Chem Phys 217:636–645
185. Iskin B, Yilmaz G, Yagci Y (2011) Synthesis of ABC type miktoarm star copolymers by triple click chemistry. Polym Chem 2:2865–2871
186. Gao C, Yan D (2004) Hyperbranched polymers: from synthesis to applications. Prog Polym Sci 29:183–275
187. Voit BI, Lederer A (2009) Hyperbranched and highly branched polymer architectures-synthetic strategies and major characterization aspects. Chem Rev 109:5924–5973
188. Kong LZ, Sun M, Qiao HM, Pan CY (2010) Synthesis and characterization of hyperbranched polystyrene via click reaction of AB2 macromonomer. J Polym Sci Part A Polym Chem 48:454–462
189. Han J, Zhu D, Gao C (2013) Fast bulk click polymerization approach to linear and hyperbranched alternating multiblock copolymers. Polym Chem 4:542–549
190. He C, Li LW, He WD, Jiang WX, Wu C (2011) “Click” long seesaw-type a ~ ~b ~ ~a chains together into huge defect-free hyperbranched polymer chains with uniform subchains. Macromolecules 44:6233–6236
191. Chen SQ, He C, Li HJ, Li PY, He WD (2016) Janus long-chain hyperbranched copolymers of PSt and POEGMA from a self-assembly mediated click reaction. Polym Chem 7:2476–2485
192. Li S, Han J, Gao C (2013) High-density and hetero-functional group engineering of segmented hyperbranched polymers via click chemistry. Polym Chem 4:1774–1787
193. Cai T, Li M, Neoh KG, Kang ET (2013) Surface-functionalizable membranes of polycaprolactone-click-hyperbranched polyglycerol copolymers from combined atom transfer radical polymerization, ring-opening polymerization and click chemistry. J Mater Chem B 1:1304–1315
194. Konkolewicz D, Gray-Weale A, Perrier S (2009) Hyperbranched polymers by thiol-yne chemistry: from small molecules to functional polymers. J Am Chem Soc 131:18075–18077
195. Xu J, Tao L, Boyer C, Lowe AB, Davis TP (2010) Combining thio-bromo Click chemistry and raft polymerization: a powerful tool for preparing functionalized multiblock and hyperbranched polymers. Macromolecules 43:20–24
196. Konkolewicz D, Poon CK, Gray-Weale A, Perrier S (2011) Hyperbranched alternating block copolymers using thiol-yne chemistry: materials with tuneable properties. Chem Commun 47:239–241
197. Barbey R, Perrier S (2014) Synthesis of polystyrene-based hyperbranched polymers by thiol-yne chemistry: a detailed investigation. Macromolecules 47:6697–6705
198. Barbey R, Perrier S (2013) A facile route to functional hyperbranched polymers by combining reversible addition-fragmentation chain transfer polymerization, thiol-yne chemistry, and postpolymerization modification strategies. ACS Macro Lett 2:366–370
199. Cai T, Li M, Zhang B, Neoh KG, Kang ET (2014) Hyperbranched polycaprolactone-click-poly(*N*-vinylcaprolactam) amphiphilic copolymers and their applications as temperature-responsive membranes. J Mater Chem B 2:814–825
200. Chang X, Dong CM (2013) Synthesis of hyperbranched polypeptide and PEO block copolymer by consecutive thiol-yne chemistry. Biomacromolecules 14:3329–3337