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EDITORIAL

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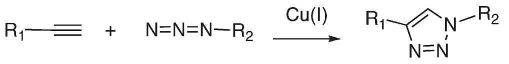
A Virtual Issue of *Macromolecules*: "Click Chemistry in Macromolecular Science"

We are delighted to announce the inaugural "virtual issue" for *Macromolecules*. A virtual issue is one in which a set of thematically related, recently published papers are collected in a Web-only edition of the journal; they may also be found directly from the *Macromolecules* Home Page (http://pubs.acs.org/page/mamobx/vi/1). All of these papers are freely accessible, even for readers without a subscription, until the next virtual issue takes its place. Our goals are to broaden access to some of the most exciting recent science in *Macromolecules*, to draw attention to the wide variety of specific topics that these related papers address, and to serve as a valuable resource to the community. In this instance, we have selected a topic that is currently generating a great deal of excitement and activity across many areas of modern polymer synthesis and applications, namely the use of so-called "click chemistry". Accordingly, we have assembled 27 papers that were published in *Macromolecules* in 2008 or in the early part of 2009, which utilize click chemistry as a tool to solve a particular synthetic or materials challenge.

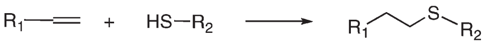
In the broadest sense, "click chemistry" may be taken to denote a reaction that has the following attributes:

- quantitative
- rapid
- no byproducts
- no side reactions
- functional group tolerant
- mild reaction conditions
- broadly applicable

Among these, the exemplary click reaction is the copper(I)-catalyzed Huisgen [3 + 2] dipolar cycloaddition between an alkyne and an azide, described by Kolb, Finn, and Sharpless as the "cream of the crop":[1]



And, although this reaction is certainly very popular, others are of importance too, including the thiol−ene reaction



and the classical Diels−Alder diene + olefin [4 + 2] cycloaddition.

Clickable groups placed at chain termini, or randomly incorporated along the backbone, provide reactive sites for postpolymerization functionalization. This strategy may allow introduction of specific functionalities that would otherwise not survive the polymerization or offer routes to prepare a family of related materials from one polymeric precursor. For example, Sinha and co-workers incorporated a propargyl-conjugated propylenedioxythiophene (ProDOT) monomer into the regioregular polymerization of ProDOT; the resulting polymer was functionalized to tune its solubility (and therefore processability) in aqueous and organic media.[2] In related work, Daugaard et al. polymerized an azide-functional 3,4-ethylenedioxythiophene (EDOT) monomer to prepare readily functionalizable conductive polymer films.[3] An analogous approach using classical diol + diisocyanate polyurethane chemistry, with alkyne-bearing diols, was reported by Fournier and du Prez.[4] Polyurethanes represent an important class of materials with many appealing and tunable properties, and the resulting linear polyurethane precursors could be functionalized in a variety of ways, for example, for specific biomedical applications. The promising tolerance of clickable groups to controlled radical polymerization also affords the opportunity to install pendant functionality in well-defined polymers, including block polymers. Fleischmann et al. used nitroxide-mediated polymerization to prepare styrene- and 4-hydroxystyrene-based diblock copolymers bearing pendant alkynes, although in this instance the alkyne was protected by a trimethylsilyl group during polymerization.[5] Zhang et al. used reversible addition/fragmentation chain transfer polymerization (RAFT) to prepare block copolymers of poly(ethylene glycol) side-chain methyl methacrylates and propargyl methacrylates.[6] A pyrenyl azide was then clicked onto the latter block to provide self-assembling polymers with interesting donor−acceptor behavior. Photosensitivity was also the goal of Gacal et al.,[7] who prepared azide-functional polystyrene backbones, to which anthracene units were appended by a "double-click" procedure involving [3 + 2] cycloaddition followed by a [4 + 2] Diels−Alder reaction.

The attributes of the azide plus alkyne click reaction make it an appealing route to chain extension and thus to block polymers that might otherwise be difficult to prepare (for example, by sequential living polymerizations). Furthermore, given sets of N complementary end-functional polymers, it is possible through one click reaction to prepare up to $N(N-1)$ distinct diblock copolymers. Urein and co-workers provide an excellent example of this strategy, clicking azide-terminal polystyrenes with ω-ethylnyl or α,ω-ethynyl poly(3-hexylthiophenes).[8] This approach can also be used to prepare $(AB)_n$ multiblocks, as demonstrated by Wang et al.[9] Commercially available hydroxyl-terminated PEO−PPO−PEO triblocks were end-functionalized with either azides or alkynes to prepare telechelic precursors. The subsequent end-to-end linking reactions were facilitated by micellization in aqueous solution, which concentrated the otherwise dilute complementary groups within the micellar PEO coronas. The value of the click approach to block polymers can be even greater when the target is a more complicated architecture, such as an ABC linear terpolymer, a miktoarm star ABC terpolymer, a cyclic AB diblock copolymer, or a linear−cycle "tadpole" diblock. Examples of these four classes were presented by Lin et al.,[10] Yuan et al.,[11] Eugene and Grayson,[12] and Dong et al.,[13] respectively.

Just as click reactions can be useful steps in the synthesis of well-defined block polymers, so too can they be effective in the preparation of branched architectures. For example, Qin et al. prepared hyperbranched polytriazoles by an A_2 (diazide) plus B_3 (triyne) polycondensation and demonstrated control over photoemission wavelength via regiochemistry.[14] Li and co-workers used an AB_2 approach, where two azides and one alkyne surrounded a central azobenzene chromophore, to prepare materials with promising nonlinear optical properties.[15] Synthesis of dendrimers, dendrons, and their related precision-branched structures can also be facilitated by judicious application of click chemistry. Shen et al. incorporated multiple azobenzene chromophores into fourth-generation dendrons, without recourse to any protection/deprotection steps.[16] Dong and co-workers prepared linear–dendron hybrid diblocks by clicking azide end-functional linear poly(ethylene oxides) with various generation dendrons of poly(ε-caprolactone)[17] or poly(γ-benzyl-L-glutamate), where the dendron core contained the necessary single alkyne moiety. Urbani et al. used a convergent click approach to prepare 3-arm stars and second-generation dendrimer-like block polymers from α-hydroxyl, ω-azido-terminal polystyrenes, poly(methyl acrylates), and poly(*tert*-butyl acrylates) with tripropargylamine.[18] A key practical advance was the use of copper wire as the click catalyst to allow facile catalyst removal and reuse.

Functionalization and stabilization of nanoparticles represents another arena with rich opportunities for click chemistry. Li and Benicewicz grew an azido-functional methacrylate polymer via surface-initiated RAFT polymerization on silica particles.[19] A given coated particle could then be functionalized in a variety of ways by reaction with appropriate alkynes. In related work, Nicolas et al. prepared random copolymers of alkyl cyanoacrylate and a PEG–side chain cyanoacrylate in organic media with azide groups at the PEG terminus.[20] The polymers self-assemble in aqueous solution, either prior to or after click functionalization with alkynes, thereby providing another convenient way to tune the synthesis. Goldmann and co-workers used both azide–alkyne and thiol–ene reactions to graft chains to the surfaces of cross-linked poly(divinylbenzene) nanoparticles.[21] Click reactions can also be useful to lock in the cores of self-assembled nanoparticles, as demonstrated by Zhang et al.[22] In this instance they employed two complementary graft copolymers with poly(*N*-isopropylacrylamide) grafts: one with an anionic backbone and one with a cationic backbone. In aqueous solution the two polymers formed polyelectrolyte complexes. As both ionomeric chains contained azido-functional comonomers, a difunctional propargyl ether cross-linked the nanoparticle cores. This strategy can also be useful in the preparation of polymer/inorganic nanocomposites. Tasdelen and co-workers demonstrated the efficacy of using alkyne-terminated poly(tetrahydrofuran) and azide-functionalized montmorillonite clay to prepare well-dispersed, thermally stable blends.[23]

At the most fundamental level of synthetic polymer chemistry, click reactions can be utilized to form new monomers, new polymers, and new macromonomers. Recent examples of all three strategies may be found in the work of Munteanu et al.,[24] Qin and co-workers,[25] and Topham et al.,[26] respectively. The first of these used click reactions to prepare cyclodextrin-modified methacrylates, either before or after radical polymerization. Interestingly, the use of microwave radiation appeared to enhance the regioselectivity of the click reaction. The last of these three studies demonstrated the facile preparation of a variety of methacrylic macromonomers, by ATRP from an azide functional initiator, followed by clicking with propargyl (meth)acrylate to yield the desired macromonomers. Mapping out the limits within which a given reaction satisfies the ideal criteria listed above is also an important fundamental goal. Ladmiral and co-workers report that azides can react with the double bonds of certain monomers, under conditions that would otherwise be appropriate for controlled radical polymerization, and suggest strategies for mitigating this difficulty.[27] In order to expand the applicability of other potential click reactions, various groups have explored the thiol–ene reaction identified above. An important recent example is the work of Campos et al.,[28] who demonstrated inter alia that the thiol–ene reaction was orthogonal to the azide–alkyne click reaction, that it could be used with both end- and side-chain double bonds, and that use of photochemical radical initiators could greatly improve the performance of the thiol–ene coupling compare to thermal initiators.

While the above-cited papers have in common the utilization of click chemistry, it is clear that they span a very wide range of synthetic and materials targets. Furthermore, the fact that they have appeared over a relatively short time span is just one indication of the vibrancy and importance of this particular focus topic. We hope that this virtual issue proves to be both interesting and useful to the community, and we welcome your feedback. In particular, we encourage suggestions for future topics and for individuals to organize virtual issues as guest editors.

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