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Cycloaddition Reactions and Dendritic Polymer Architectures – A Perfect Match

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Summery: The potential of cycloaddition (CA) reactions for the synthesis of dendritic polymers is pointed out. The [4 + 2] Diels Alder cycloaddition as well as 1,3-dipolar CA reactions including "click chemistry" are addressed, and the advantages of these reactions like high selectivity, thus high tolerance towards additional functionalities, high yields and synthesis under mild reaction conditions are highlighted. New perfectly branched dendrimers as well as hyperbranched polymers have been prepared and modified using the 1,3-dipolar cycloaddition reaction of azines with alkynes. The 1,3-dipolar CA reaction of bisazine with maleimides results in hyperbranched and thus, irregular and broadly distributed polymers though with a degree of branching of 100% due to special intermediate formation. The [4 + 2] Diels Alder cycloaddition was successfully applied for the synthesis of highly branched polyphenylene structures using the $AB_2 + AB$ and the $A_2 + B_3$ approach. CA reactions are also very suitable for highly efficient polymer analogous reactions and thus, they can also be used to prepare complex polymer architectures like dendronized polymers.

Keywords: cycloaddition reactions; dendritic polymers; dendronized polymers; hyperbranched polymers; polymer analogous reaction

Introduction

Dendritic polymers, the perfectly branched dendrimers as well as their hyperbranched cousins and a variety of combinations between dendritic and linear structures, are certainly among the most studied functional and specialty polymers today. Due to the highly branched, compact and highly functional structure with special reactivity, solubility and rheology features, applications in nanotechnology, biomedicine, sensorics, and micro(nano)electronics, but also in a variety of reactive formulations are discussed. The reactions explored so far for the synthesis of dendritic polymers are numerous and covered in a number of excellent reviews.[1–4] Cycloaddition (CA) reactions are known to exhibit the features needed urgently in dendrimer synthesis: They are very efficient and highly selective and allow even stereoselectivity with the potential to form special intermediates controlling e.g. the degree of branching. These reactions have been used successfully in polymer synthesis already for 40 years,[5] an area reviewed excellently very recently by Goodall and Hayes[6] who already pointed out the developments in dendrimer synthesis.[7–9]

However, only recently, especially with further developments concerning the Huisgen 1,3-dipolar cycloaddition[10] towards the so-called "click chemistry"[11], the use of CA reactions has grown nearly exponentially, for both the preparation and functionalization of dendrimers and dendrimer-linear hybrids.[12]

In this respect, our own activities in this field using 1,3-dipolar CA (alkyne + azide or bisazine + maleimide) as well as the [4 + 2] Diels Alder CA (cyclopentadienone +

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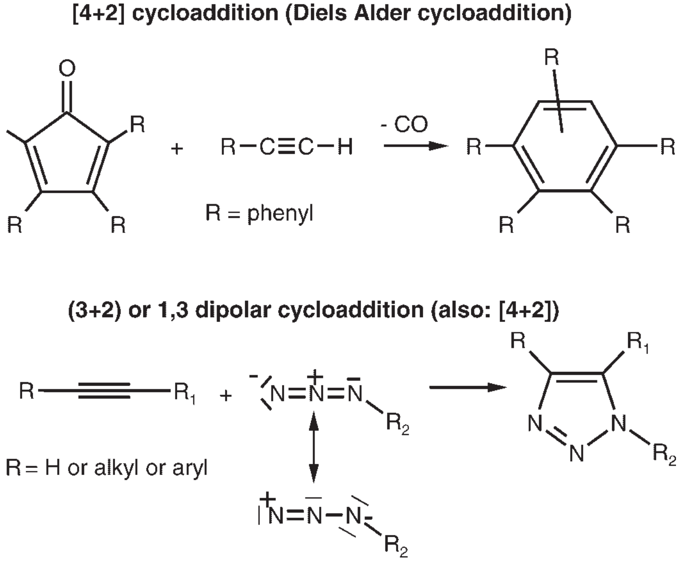


Scheme 1.
Cycloaddition reactions used.

alkyne) will be reviewed here. Scheme 1 exemplifies the mainly used reactions schematically.

Experimental Part

Details regarding synthesis and characterization of the described highly branched products can be found in the respective publications.[13–19]

Results and Discussion

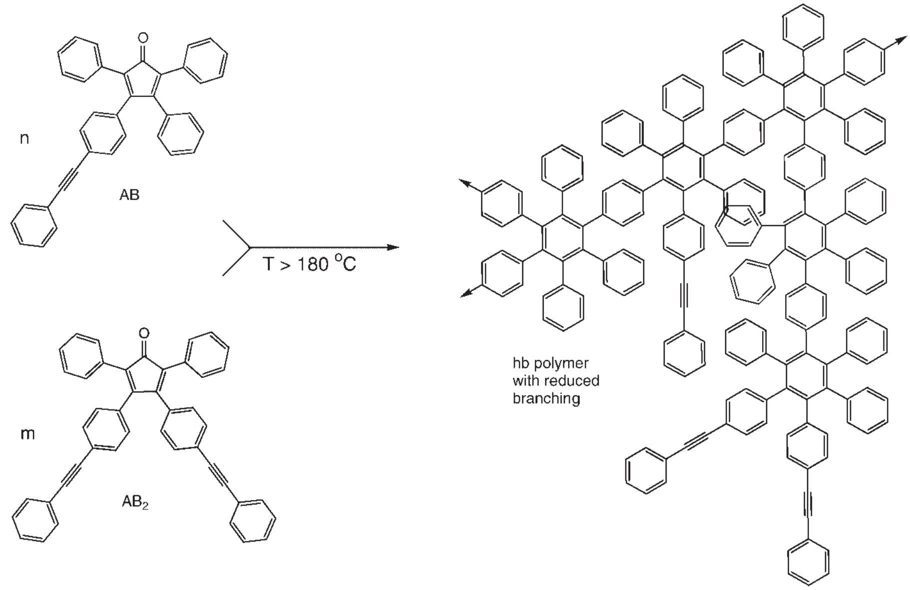
Cycloaddition Reactions and Polyarylenes

Polyphenylenes are an interesting class of materials due to a usually high thermostability and chemical inertness. Furthermore, the highly aromatic nature renders these structures suitable for a number of technological applications e.g. in microelectronics implying also the potential to include controllable conductive behavior. Introducing branched units allows to overcome a major drawback of these structures, which is the limited processability, and thus polyphenylene dendrimers based on the Diels Alder reaction had been the issue of one of the first reports on the use of CA reactions in dendrimer synthesis.[7–9] This synthetic approach is based on the cycloaddition of phenylated cyclopentadienones with phenylated alkynes and subsequent decarbonylation (Scheme 1). By now a vast number of polyphenylene dendrimers with a dense packing or a more extended arrangement of benzene rings, but also including additional extended or asymmetric structural units and a variety of functional surface groups has already been prepared and characterized.[7–9,20] In addition, further oxidative cyclohydrogenation of the discussed polyphenylenes allows the construction of polycyclic hydrocarbon architectures,[21] and also the preparation of graphite-analogue thin layers and carbon nanotubes has been reported.

Not only the perfectly branched dendrimers, but also hyperbranched polyphenylenes had been explored. In general, polyphenylenes possess a high thermal and chemical stability. However, in contrast to their linear analogues, the hyperbranched polyphenylenes are non-conducting polymers, because an extended π-conjugation is hindered due to their tightly packed and strongly twisted phenylene units. They show good solubility and processability comparable to those of the corresponding dendrimers, but are more easily available also in larger quantities. Due to the outlined properties hyperbranched polyphenylenes are promising candidates for the application as insulating materials in microelectronics, where features like high thermal stability, good processability and solubility and low moisture absorption are required. An example for a low-dielectric-constant polymer based on branched and crosslinked polyarylenes which is already used by the semiconductor industry is SiLK™ from The Dow Chemical Company.[22] Morgenroth and Müllen[23] reported e.g. the Diels-Alder reaction of suitable AB_2 monomers.

This approach has been extended recently by us combining the AB_2 monomer 3,4-bis-(4-(phenylethynyl)phenyl)-2,5-diphenylcyclopentadienone as reported by Morgenroth and Müllen[23] with an AB monomer; the reaction was carried out in diphenylether at 230 °C (Scheme 2).[12,13] Besides giving some control over the degree of branching in the branched polyphenylenes, the addition of the AB monomer e.g. in a 3:1 (AB_2: AB) ratio limited the achievable molar masses to some extent: $\overline{Mw}$ values of up to 75,000 g/mol were obtained compared to up to 600,000 g/mol for pure AB_2 monomer used under identical reaction conditions. Unfortunately, even though all the repeating units - linear, dendritic and terminal - could be identified and proven, a quantification e.g. by ^{13}C NMR analysis is not possible due to overlapping signals, and thus, no quantitative information on the degree of branching can be given. The achievement of high molar masses with relatively broad molar mass distributions ($\overline{Mw}/\overline{Mn}$ between 3 and 30) and rather multimodal GPC traces combined with an excellent solubility e.g. in chloroform or toluene are further indications for a highly branched nature of the products. In addition, solid state[24] and solution[14] NMR studies proved hindered dynamics in the dendritic polyphenylenes as a result of the dense packing of the phenylene rings.

There are two ways to prepare hyperbranched polymers: the classical "Flory"



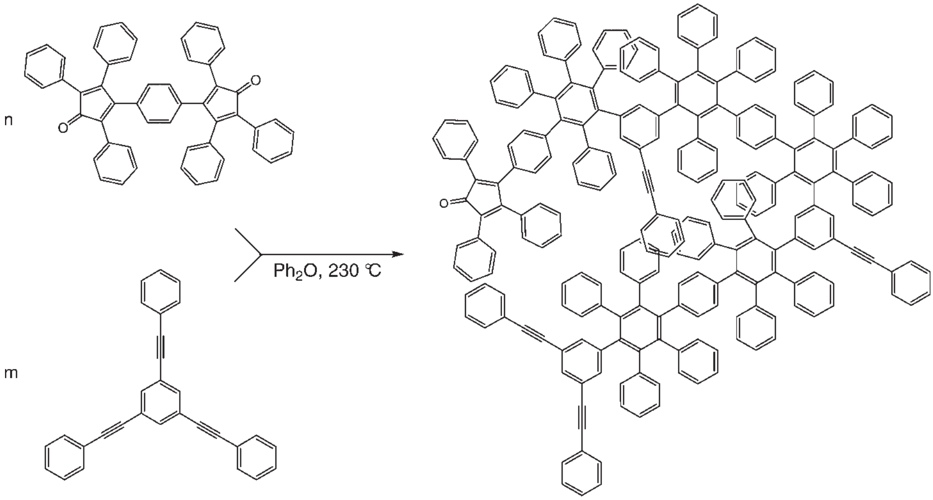
Scheme 2.
Synthesis of hyperbranched polyphenylenes with an increased fraction of linear units by Diels Alder reaction from AB_2 and AB monomers [reprinted with permission from NJC].[12,13]

approach using AB_x type monomers as a non-gelating system, and the more simple A_2+B_3 approach which allows the use of more easily available monomers but implies the possibility of gelation which is only avoided by restriction of the conversion or high imbalance of the stoichiometry. Nevertheless, also through the $A_2 + B_3$ approach fully soluble hyperbranched polyphenylenes via the Diels Alder reaction have been prepared[13] following the route demonstrated extensively by Müllen et al.[9] Scheme 3 indicates the monomers used. It is interesting to note that by this monomer combination a higher sterical hindrance was achieved in the final polymer structures compared to the hyperbranched polyphenylenes prepared by the AB_2 monomers. Thus, detailed NMR investigations[14] revealed that the formation of linear units is favored since the reactivity of the third B unit in B_3 after two Bs have already reacted is reduced. Only when a high excess of A_2 is applied the formation of dendritic units becomes more significant, however, then the achievable molar mass is limited. An advantage of this fact is that also the critical conversion is shifted by this reduced reactivity, and thus only fully soluble products were obtained under the applied conditions.

Complex Dendritic Architectures by 1,3-dipolar Cycloaddition Reactions

Whereas the above outlined Diels Alder reactions are especially well suited to prepare highly aromatic hydrocarbon structures which exhibit high shape-persistancy and usually a more non-polar character, the 1,3-dipolar cycloaddition reactions offer the possibility to prepare complex heterocycles and also to introduce polar functionalities. In addition, depending on the reaction mechanism and the reaction conditions, a high stereocontrol is possible and the formation of specific intermediates may allow to influence the degree of branching. Usually very high yields can be achieved, however, this high reactivity of the starting compounds can also lead to adverse side reactions between the 1,3-dipoles such as dimerizations and rearrangements (e.g. sigmatropic shifts), and therefore, the reaction conditions have to be selected carefully.

Our first approach[15,16] used so far for the preparation of dendritic structures is based on the so-called "criss-cross"



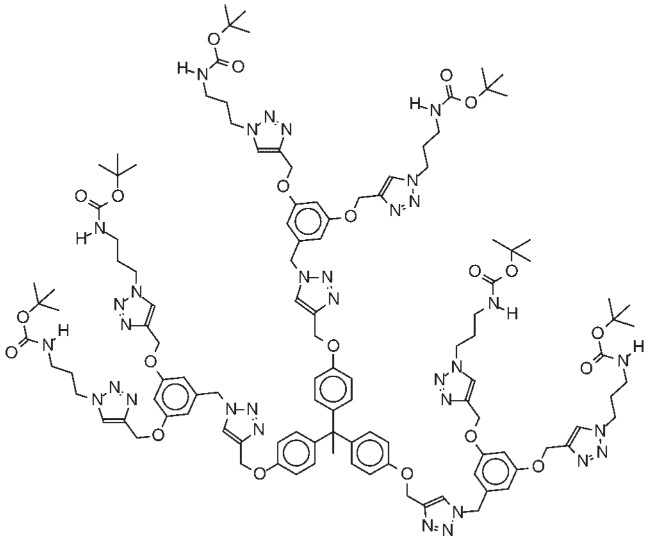
Scheme 3.
Synthesis of hyperbranched polyphenylenes following the $A_2 + B_3$ approach (Diels Alder reaction) [reprinted with permission from NJC].[12,13]

cycloaddition of bisazines which always react in a two step dual $(3+2)$ cycloaddition via an instable azomethinimine 1,3-dipole intermediate.[25] For preparing hyperbranched polymers, an AB_2 monomer containing the bisazine moiety (B_2 unit) as well as a maleimide function (A unit) was designed and synthetically realized.[15] Due to the special features of that reaction and the instable azomethinimine intermediate it was possible to achieve hyperbranched polymers without any linear units and therefore featuring a degree of branching of 100%. In the first reaction of the maleimide with one of the azine units an instable azomethinimine cyclic system is formed as a linear unit which can only go forward by reacting with the second azine to form a stable tetracyclic system or to go backwards to the starting material. Since the linear units are not stable, they cannot be found in the final product and only bisazine terminal units as well as tetracyclic fully dendritic units were determined leading to a formal DB of 100%. These structural features and thus, the absence of any linear units could also be proven by detailed NMR analysis and by the use of model compounds despite the rather high number of isomers found in the tetracyclic systems.[16] Nevertheless, irregularly branched products of molar masses $\overline{Mw}$ up to 10,000 g/mol and polydispersities around 2.5 were isolated and certainly qualified as "hyperbranched".

As one can expect, the 1,3-dipolar CA reaction of azides and alkynes also entered quickly the field of dendritic polymers. The potential given by the combination of "click chemistry" and dendritic structures is greatly demonstrated by the groups of Hawker and Sharpless.[17]

We could show the direct build up of dendrons of different generations by a convergent approach using the 1,3-dipolar cycloaddition reaction of azides with terminal alkynes as well as various highly efficient CA end group modification reactions in order to introduce functionality in the periphery. Scheme 4 presents one of our low generation examples.

But of course, the "click chemistry" can also be used for the preparation of novel hyperbranched polymers. The synthesis of hyperbranched poly([1,2,3]-triazole)s via 1,3-dipolar cycloaddition was successfully achieved with the AB_2 monomer 3,5-bis(propargyloxy)benzyl azide, having an

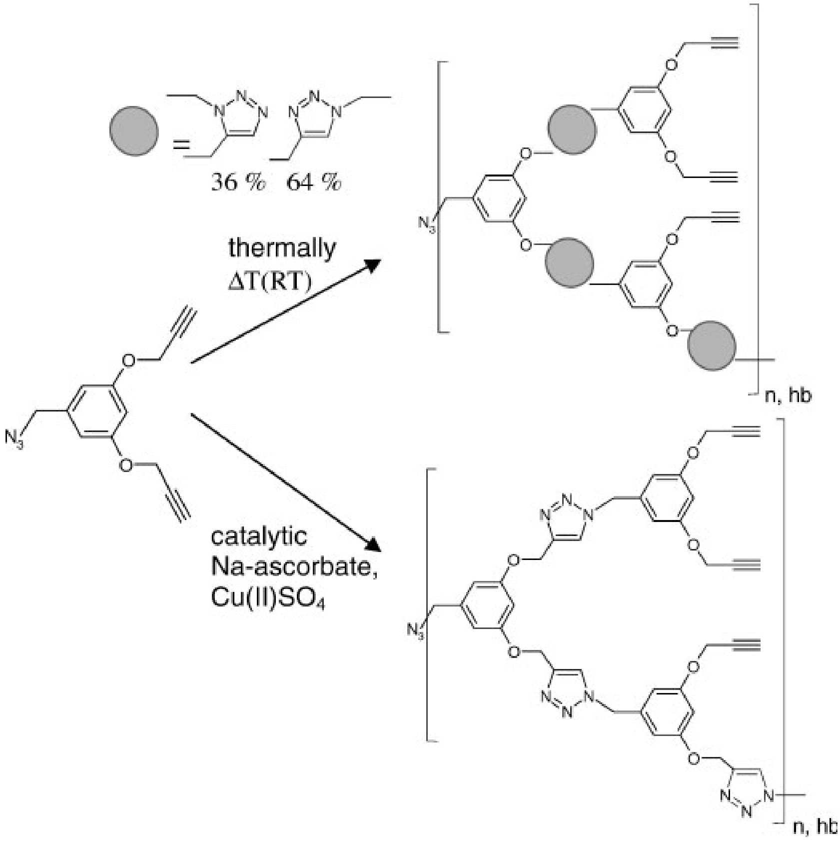


Scheme 4.
End-functionalized poly([1,2,3]-triazole) dendrimer of generation 1 prepared by "click chemistry" [reprinted with permission from NJC].[12,17]

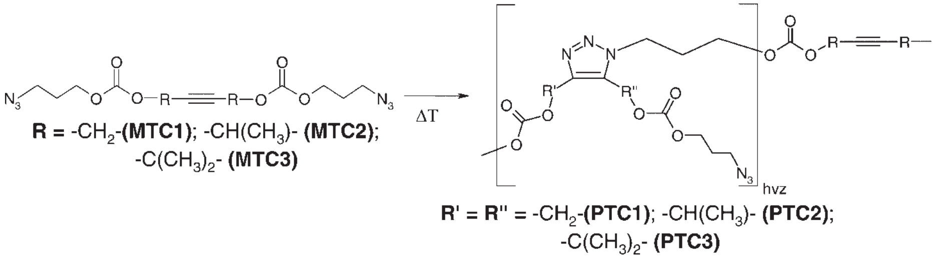
azide group as A-unit and two terminal triple bonds as B units (AB_2-bisalkyne).[18]

The polymerization of the AB_2-bisalkyne was either conducted via thermal polymerization or under copper(I) catalysis (Scheme 5). The latter leads to insoluble products under the chosen reaction conditions (room temperature), probably due to the very high molar masses achieved and maybe also due to the occurrence of side reactions. However, full stereo-control of the formed triazole units was maintained and only 1,4-substituion in the triazole ring as well as a degree of branching of 50%, which is typical for a random and ideal AB_2 condensation, was confirmed ^1H and ^{13}C HR-MAS NMR spectroscopy of the swollen samples. By autopolymerization at room temperature fully soluble products of high molecular weight could be obtained from the AB_2-bisalkyne but the regioselectivity was lost (Scheme 5). The 1,4- and 1,5-substitution in the triazole ring were found in a 64:36 ratio.

Bisazides with internal triple bonds as AB_2 monomers for the synthesis of hyperbranched poly([1,2,3]-triazole)s have independently been developed by us[18,19] and Smet et al.[26] Here one has to note that the high stereocontrol achieved by the Cu^I catalyzed ''click chemistry'' does not apply for substituted alkynes. Thus, only a classical thermally induced 1,3-dipolar CA reaction will occur leading again to a mixture of 1,4- and 1,5-substituted triazoles. Smet et al.[26] studied some ester-alkyne-diazides reaching only oligomers and products showing a tendency to gel after



Scheme 5.
Preparation of hyperbranched poly([1,2,3]-triazole)s via thermal and Cu^I mediated 1,3-dipolar CA of 3,5-bis(progargyloxy)benzyl azide [reprinted with permission from NJC].[12,18]



Scheme 6.
Synthesis of hyperbranched poly([1,2,3]-triazole)s PTC1-3 from the AB_2 bisazide carbonates MTC1-3 via thermal 1,3-dipolar CA [reprinted with permission from NJC].[12,18]

storage, probably because of some decomposition of the azide groups. We were, however, able to achieve fully soluble products by low temperature (45 °C) autopolymerization in bulk even of high molar mass ($\overline{Mn} = 10{,}000$ g/mol) from the AB_2 bisazide monomer MTC1 shown in Scheme 6.

Full structural analysis is complex due to the large number of possible isomeric structural units, but the highly branched structure could be verified in the products and a degree of branching of 50% can be assumed. The resulting product bears a large number of highly reactive azide groups which can give rise to a large spectrum of further end group modification. Here, it is most suitable to use the reaction with functional terminal alkynes again for the postmodification due its easy and highly efficient character. Thereby it was possible to introduce a variety of polar and non-polar end groups which allow firstly to avoid any side reactions of the azide units and secondly, to adjust the polarity of the material e.g. in order to achieve better solubility in non-polar solvents.[19] Polymers based on MTC1-3 have aliphatic carbonate groups in their structure. Aliphatic carbonates are known to decompose readily at temperatures around 200 °C. This makes these hyperbranched polymers promising materials e.g. for the use as porogens for the preparation of nanoporous materials, but this also requires to find a suitable solvent for both, porogen and matrix material, for the successful preparation of homogenous films.[18]

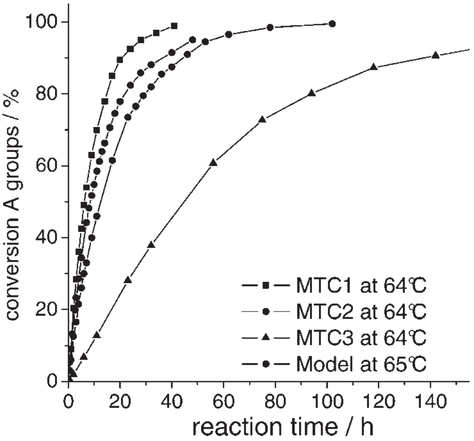
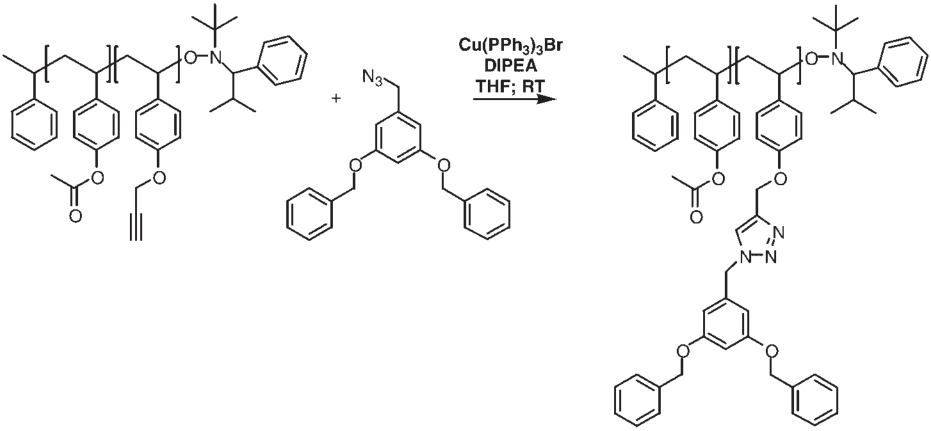


Figure 1.
Dependency of the conversion of A groups on the reaction time for the different AB_2 bisazide carbonates MTC1-3. The model reaction is based on the addition reaction of 3-azidopropanol to 1,4-diacetoxy-but-2-ine [reprinted with permission from NJC].[12]



Scheme 7.
Polymer analogous "click" CA reaction for the preparation of dendronized block copolymers.

In more extended studies[19] it was finally possible to optimize the reaction conditions, and soluble products could be obtained for MTC2 and MTC3, too. The reactivity of these two compounds is significantly lower than the one of MCT1 as it was found in some kinetic studies (Figure 1) carried out at 64 °C.

For MTC3 the reaction temperature should not be increased above 45 °C due to the high thermolability of the carbonate units and thus some degradation was observed during the kinetic experiment at 64 °C. However, at 45 °C reaction times of up to 4 weeks had to be employed to achieve high molar mass products. The evaluation of the data achieved at 64 °C for first and second order kinetics showed, that in this AB_2 CA reaction none of these plots followed ideal linear behavior. Best fitting of the kinetics could be achieved by two parallel reactions of first and second order with the polymerization by intermolecular reaction of A and B groups as the second order reaction. Detailed evaluation of this behavior and also a very close study of the accompanying development of the molar masses and the polydispersity led to the conclusion that internal cyclization (first order reaction) takes place to a significant proportion at high conversions of the functional group. It has to be noted that during these studies it could be verified that soluble products with $\overline{Mn}$ up to 38,000 g/mol and $\overline{Mw} = 100{,}000$ g/mol (MALLS detection) can be produced from MTC1.

The high efficiency of the "click reactions" of alkynes with azides and the easy introduction of the suitable starting units into polymer chains also qualifies this reaction strongly for the use in polymer analogous reactions for the preparation of complex polymer architectures. Thus we started to prepare block copolymers having alkyne units in one segment and reacted those with azide containing dendrons to yield dendronized block copolymers as outlined in Scheme 7.[27]

Conclusion

Cycloaddition reactions entered, with a few exceptions, only recently the field of dendritic polymers. Nevertheless, due to the resulting high yields, high selectivity, very clean reactions and often the absence of any side reaction, they proved already extremely versatile and ideal for the effective dendrimer synthesis as well as highly efficient for the postmodification of highly functional dendritic macromolecules. Especially two types of reactions are very promising: the Diels Alder reaction of cyclopentadienone with alkynes leading to a large variety of polyphenylene dendrimers otherwise very difficult to realize and the 1,3-dipolar cycloaddition reaction of azides with alkynes. The latter allows not only the preparation of entirely new dendritic structures, it is also very efficient concerning the introduction of complex functionalities into dendritic structures.

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[1] G. R. Newkome, C. N. Moorefield, F. Vögtle, "*Dendrimers and Dendrons: Concepts, Synthesis, Applications*", Wiley-VCH, Weinheim 2001.

[2] J. M. J. Fréchet, D. A. Tomalia, "*Dendrimers and Other Dendritic Polymers*", John Wiley & Sons, Chichester UK 2001.

[3] C. Gao, D. Yan, *Prog. Polym. Sci.* **2004**, *29*, 183.

[4] B. Voit, *J. Poly. Sci. Part A: Polym. Chem.* **2005**, *43*, 2679.

[5] J. K. Stille, T. Anyos, *J. Polym. Part A: Sci. Polym. Chem.* **1964**, *2*, 1487.

[6] G. W. Goodall, W. Hayes, *Chem. Soc. Rev.* **2006**, *35*, 280.

[7] M. Müller, H. Mauermann-Düll, M. Wagner, V. Enkelmann, K. Müllen, *Angew. Chem. Int. Ed* **1995**, *34*, 1583.

[8] F. Morgenroth, E. Reuther, K. Müllen, *Angew. Chem.* **1997**, *109*, *647; Angew. Chem. Int. Ed.* **1997**, *36*, 631.

[9] A. J. Berresheim, M. Müller, K. Müllen, *Chem. Rev.* **1999**, *99*, 1747.

[10] R. Huisgen, G. Szeimies, L. Möbius, *Chem. Ber.* **1967**, *100*, 2494.

[11] V. V. Rostovtsev, L. G. Green, V. V. Fokin, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2002**, *41*, 2596.

[12] B. Voit, *New J. Chem.* **2007**, (Advance Article) DOI: 10.1039/b615637c.

[13] K. Stumpe, H. Komber, B. Voit, *Macromol. Chem. Phys.* **2006**, *207*, 1825.

[14] H. Komber, K. Stumpe, B. Voit, *Macromol. Chem. Phys.* **2006**, *207*, 1814.

[15] G. Maier, C. Zech, B. Voit, H. Komber, *Macromol. Chem. Phys.* **1998**, *199*, 2655.

[16] G. Maier, C. Zech, B. Voit, H. Komber, *Macromol. Sym.* **2001**, *163*, 75.

[17] P. Wu, A. K. Feldman, A. K. Nugent, C. J. Hawker, A. Scheel, B. Voit, J. Pyun, J. M. J. Fréchet, K. B. Sharpless, V. V. Fokin, *Angew. Chem. Int. Ed.* **2004**, *43*, 3928.

[18] A. Scheel, H. Komber, B. Voit, *Macromol. Rapid Commun.* **2004**, *25*, 1175.

[19] A. Scheel, *Thermisch labile hochverzweigte Polycarbonate und Poly([1,2,3]-triazolcarbonat)e (PhD Thesis Technische Universität Dresden)*, Verlag Dr. Hut, München, **2006**.

[20] A. C. Grimsdale, K. Müllen, *Angew. Chem. Int. Ed.* **2005**, *44*, 5592.21 L. Zhi, J. Wu, J. Li.

[21] M. Stepputat, U. Kolb, K. Müllen, *Adv. Mater.* **2005**, *17*, 1492.

[22] S. J. Martin, J. P. Godschalx, M. E. Mills, E. O. Shaffer, II, P. H. Townsend, *Adv. Mater.* **2000**, *12*, 1769.

[23] Morgenroth, K. Müllen, *Tetrahedron* **1997**, *53*, 15349.

[24] M. Wind, U.-M. Wiesler, K. Saalwächter, K. Müllen, H. W. Spiess, *Adv. Mater.* **2001**, *13*, 752.

[25] R. Huisgen, *Angw. Chem. Int. Ed.* **1963**, *2*, 565.

[26] M. Smet, K. Metten, W. Dehaen, *Collect. Czech. Chem. Commun.* **2004**, *69*, 1097.

[27] S. Fleischmann, H. Komber, B. Voit, in preparation.