Cite this: Chem. Commun., 2012, 48, 1036–1038

COMMUNICATION

Synthesizing amphiphilic block copolymers through macromolecular azo-coupling reaction[†]

Yaning He,* Wei He, Renbo Wei, Zhen Chen and Xiaogong Wang*

Received 13th October 2011, Accepted 14th November 2011 DOI: 10.1039/c1cc16362k

This communication reports a new approach to synthesize amphiphilic block copolymers. The copolymers with well-defined structures were synthesized by macromolecular azo-coupling reaction between the diazonium salt of aniline-functionalized PEG and the polymeric blocks with a terminal suitable for the azo-coupling reaction.

Block copolymers, which are composed of two or more homopolymer chains linked by covalent bonds, have been extensively investigated in recent years.¹⁻³ The unique architecture and properties of block polymers promise the realization of many potential nanotechnological applications such as semiconductor arrays, nanoscale templating and nanoscale separations.¹ The amphiphilic block copolymers, consisting of hydrophilic and hydrophobic blocks, can self-assemble in selected solvents to form various polymeric aggregates such as spherical micelles, vesicles and nanotubes, which can be used in drug delivery systems, nanoreactors and others.² In recent years, block copolymers have been prepared by various living/ controlled polymerization methods, such as living cationic or anionic polymerizations, atom transfer free radical polymerization (ATRP), reversible addition fragmentation chain transfer (RAFT) polymerization, and ring-opening metathesis polymerization (ROMP).³ The use of macroinitiators is a typical synthetic strategy to obtain block copolymers through the controlled radical polymerization. However, in some cases, the macroinitiators show less reactivity and are hard to completely form block copolymers. Therefore, new synthetic strategies are needed to obtain block copolymers, especially amphiphilic block copolymers, through other feasible approaches.

Recently, it has been reported that polymeric building blocks can be modularly synthesized *via* "click" chemistry.⁴ One obvious advantage of this approach is that the blocks before the coupling reaction can be well characterized. On the other hand, this approach needs reactive end groups to guarantee the high yield coupling reaction and avoid possible side reactions. A typical "click" reaction is 1,3-dipolar

cycloaddition between polymeric blocks bearing functional terminal azide and alkyne functionalities using copper(1) as the catalyst, which has attracted considerable attention and been applied for linking different polymeric blocks.^{4,5} Finding other high-efficient coupling reactions is a necessary step to further develop this synthetic strategy. Azo-coupling reaction is widely used in the synthesis of dyes and pigments. In these reactions, aromatic diazonium cations can efficiently react with anilines or phenols with high yield. Recently, the postpolymerization azo-coupling scheme has been developed to introduce various azo chromophores through the azo-coupling reactions between precursor polymers with anilino moieties and diazonium salts in polar organic solvents.⁶ The reaction scheme shows high efficiency and can produce azo polymers with high degree of functionalization. For the azo-coupling reaction, no catalyst and particular protection are needed. Although similar reaction can also be expected for the synthesis of various amphiphilic block copolymers, to our knowledge, no successful example has been reported in the literature yet.

In this communication, we report a novel modular strategy for the synthesis of amphiphilic block copolymers by macromolecular azo-coupling reaction between the diazonium salt of aniline-functionalized poly(ethylene glycol) (PEG) and another polymer block with a terminal suitable for the azo-coupling reaction. PEG has good water solubility and can be commercially purchased with exact molecular weight. It has been widely used as a hydrophilic block in preparing amphiphilic block copolymers.

The synthetic route of aniline-functionalized PEG is shown in Scheme 1. In the synthetic route, the tosylate ended PEG was firstly synthesized by the esterification between poly-(ethylene glycol) monomethyl ether and 4-toluenesulfonyl chloride. Aniline-functionalized PEG was then obtained by nucleophilic substitution reaction between the synthesized PEG tosylates and p-aminobenzoic acid. The synthesis details are given in ESI.[†] Another block with a terminal suitable for azo-coupling reaction was obtained from ATRP initiator 1, which was synthesized by esterification between 2-(N-ethylanilino)ethanol and 2-bromoisobutyryl bromide with high yield. Through ATRP with the initiator, hydrophobic blocks with the terminal functional group could be easily obtained. In this study, both polystyrene (PS) and poly(methyl methacrylate) (PMMA) were used to demonstrate the feasibility of this approach (Scheme 1).

Department of Chemical Engineering, Laboratory for Advanced Materials, Tsinghua University, Beijing 100084, P. R. China. E-mail: heyaning@mail.tsinghua.edu.cn, wxg-dce@mail.tisnghua.edu.cn † Electronic supplementary information (ESI) available: Synthetic procedures, experimental details and GPC curves. See DOI: 10.1039/ clcc16362k



Scheme 1 Preparation of aniline-functionalized poly(ethylene glycol) and polymers with a terminal suitable for the azo-coupling reaction, which was obtained by utilizing functionalized ATRP initiator **1**.

Azo coupling reactions were carried out between the diazonium salt of aniline-functionalized PEG (PEG-NH2) and PS or PMMA block with terminal functional groups in organic solvents. The diazonium salt of aniline-functionalized PEG was prepared by adding NaNO₂ aqueous solution into the mixture of PEG-NH₂ and HCl in water cooling with ice bath. Then azo-coupling reaction was carried out in DMF for the PS block as a typical example (Scheme 2). A similar reaction for the PMMA block is given in ESI.[†] In order to drive the azo-coupling reaction to completion, excess of aniline functionalized PEG was used. The excess of PEG could be easily removed by washing with methanol in this case. With this simple separation method, the applicability of the methodology could be limited to asymmetric diblock copolymers with high hydrophobic block content. To extend this methodology to the synthesis of other diblock copolymers, more efficient methods to remove the unreacted PEG component might be required. On the other hand, for blocks with less hydrophobicity, the azo-coupling reaction could be more efficient. In this case, using slight excess of the diazonium salt of anilinefunctionalized PEG could be the alternative option.

Fig. 1 shows the typical traces of aniline-functionalized PEG (PEG–NH₂), functionalized PS block (PS–N–Ph) and the diblock copolymer (PEG-*b*-PS). Here, the calculated molecular weights from GPC of PEG–NH₂, PS–N–Ph, and resulted PEG-*b*-PS are 3700, 8800, and 10 000, respectively. From the GPC traces, it can be seen that no residual mono-block remains after the macromolecular azo-coupling reaction. The significant shift in the GPC trace towards higher molecular weight indicates the formation of block copolymers linked by the azobenzene bridge. For the terminal-functionalized PMMA, the similar GPC result



Fig. 1 Typical GPC traces of aniline functionalized PEG (PEG–NH₂) (PDI = 1.08, $M_n = 3700$), terminal-functionalized PS (PS–N–Ph) (PDI = 1.29, $M_n = 8800$) and the coupled diblock copolymer PEG-*b*-PS (PDI = 1.27, $M_n = 10000$).

was obtained after macromolecular azo-coupling reaction (Fig. S3, ESI[†]). The typical molecular weights of PEG-NH₂, PMMA-N-Ph, and resulted PEG-b-PMMA from GPC are 3700, 14000, and 15400, respectively. The PDI of the block copolymers is almost the same as the terminal-functionalized PS or PMMA block. For example, the PDI of the functionalized PS is 1.29 and the resulted block copolymer PEG-b-PS is 1.27. The formation of the azobenzene linkage can be confirmed by the UV-Vis spectra of the diblock copolymer. Fig. 2 shows the typical UV-Vis spectra of the coupled diblock copolymer PEG-b-PS and a corresponding azobenzene derivative in THF. The synthesis of the azobenzene derivative is also given in Scheme 2. It can be seen that they have a similar absorption band position. The curves showed typical absorption behavior of the pseudo-stilbene type of azo chromophores, e.g. bands corresponding to the π - π * transition appear at longest wavelength and chromophores exhibit absorption in the visible region. Above results all indicate that the coupling reactions occur between the two blocks with the high conversions for both PS and PMMA.

Above reaction scheme can be extended to prepare polymers with different topographic shapes. A "Y" shaped amphiphilic block copolymer was prepared by using this macromolecular azo-coupling reaction scheme to demonstrate the concept. As shown in Scheme 3, the terminal functionalized polymer with two PS blocks (PS–N(Ph)–PS) was prepared by ATRP utilizing the functionalized initiator **2**, which was synthesized by



Scheme 2 Preparation of block copolymer PEG-*b*-PS and corresponding azobenzene derivative *via* azo-coupling reaction.



Fig. 2 Typical UV-Vis spectra of the diblock copolymer PEG-*b*-PS and a corresponding azobenzene derivative (AZO-M) in THF.



Scheme 3 Preparation of "Y" shaped block copolymer PEG-*b*-PS *via* macromolecular azo-coupling reaction.

esterification between N.N-diethanolaniline and 2-bromoisobutyryl bromide. After the azo coupling reaction with diazonium salts of PEG-NH₂, the "Y" shaped amphiphilic block copolymer was obtained. Similarly, the shift in the GPC trace towards higher molecular weight was observed, which verified that the macromolecular azo-coupling reaction occurred (Fig. S5, ESI⁺). However, it can be seen from the figure that the unreacted residue (PS-N(Ph)-PS) exists after the reaction. This result indicates that the position of the group suitable for the azocoupling reaction in the macromolecular chain has a significant effect on the efficiency of macromolecular azo-coupling reaction. When the group is at the end of a polymeric chain, it is easy for the macromolecular diazonium salt to attack it and the azocoupling reactions are easily carried out to completion. On the other hand, because of the steric hindrance, there is some difficulty for the macromolecular diazonium salt to attack the positions in the middle part of the macromolecular chain. In this case, an efficient way to separate the product from the unreacted mono-blocks will be required.

In conclusion, we have demonstrated a new approach for the synthesis of amphiphilic diblock copolymers *via* macromolecular azo-coupling reaction between the diazonium salt of aniline-functionalized PEG and another polymer block with a terminal group suitable for the azo-coupling reaction. The coupling can be carried in organic solvents under extremely mild conditions. Amphiphilic block copolymers with well-defined structures can be prepared through this approach. The reaction scheme can be extended to the synthesis of amphiphilic copolymers with other topographic shapes although the conversion can be affected by the functional group position.

This work was supported by Natural Science Foundation of China (21074065 and 91027024).

Notes and references

- For reviews, see: (a) I. W. Hamley, Developments in Block Copolymer Science and Technology, John Wiley & Sons Ltd, UK, 2004, pp. 1–125; (b) N. Hadjichristidis, S. Pispas and G. Floudas, Block Copolymers, John Wiley & Sons Inc, New Jersey, 2003, pp. 2–172; (c) V. Abetz and P. F. W. Simon, Adv. Polym. Sci., 2005, 189, 125; (d) S. B. Darling, Prog. Polym. Sci., 2007, 32, 1152; (e) M. R. Bockstaller, R. A. Mickiewicz and E. L. Thomas, Adv. Mater., 2005, 17, 1331; (f) C. Park, J. Yoon and E. L. Thomas, Polymer, 2003, 44, 6725; (g) J. Bang, U. Jeong, D. Y. Ryu, T. P. Russell and C. J. Hawker, Adv. Mater., 2009, 21, 1.
- 2 For example, see: (a) L. Zhang and A. Eisenberg, Science, 1995, 268, 1728; (b) B. M. Discher, Y. Y. Won, D. S. Ege, J. C. M. Lee, F. S. Bates, D. E. Discher and D. A. Hammer, Science, 1999, 284, 1143; (c) D. E. Discher and A. Eisenberg, Science, 2002, 297, 967; (d) S. Jain and F. S. Bates, Science, 2003, 300, 460; (e) K. Kita-Tokarczyk, J. Grumelard, T. Haefele and W. Meier, Polymer, 2005, 46, 3540; (f) M. Antonietti and S. Forster, Adv. Mater., 2003, 15, 1323; (g) A. Rosler, G. W. M. Vandermeulen and H. A. Klok, Adv. Drug Delivery Rev., 2001, 53, 95; (h) A. Blanazs, S. P. Armes and A. J. Ryan, Macromol. Rapid Commun., 2009, 30, 267; (i) B. M. Rossbach, K. Leopold and R. Weberskirch, Angew. Chem., Int. Ed., 2006, 45, 1309; (j) J. M. Spruell and C. J. Hawker, Chem. Sci., 2011, 2, 18; (k) C. Tonhauser, B. Obermeier, C. Mangold, H. Löwe and H. Frey, Chem. Commun., 2011, 47, 8964; (1) D. Zehm, A. Laschewsky, P. Heunemann, M. Gradzielski, S. Prévost, H. Liang, J. P. Rabe and J. F. Lutz, Polym. Chem., 2011, 2, 137.
- 3 For example, see: (a) J. S. Wang and K. Matyjaszewski, J. Am. Chem. Soc., 1995, 117, 5614; (b) J. Chiefari, Y. K. Chong, F. Ercole, J. Krstina, J. Jeffery, T. P. T. Le, R. T. A. Mayadunne, G. F. Meijs, C. L. Moad, G. Moad, E. Rizzardo and S. H. Thang, Macromolecules, 1998, 31, 5559; (c) S. B. T. Nguyen, L. K. Johnson, R. H. Grubbs and J. W. Ziller, J. Am. Chem. Soc., 1992, 114, 3974; (d) G. Moad, E. Rizzardo and D. H. Solomon, Macromolecules, 1982, 15, 909; (e) M. Szwarc, M. Levy and R. Milkovich, J. Am. Chem. Soc., 1956, 78, 2656.
- 4 For example, see: (a) H. C. Kolb, M. G. Finn and K. B. Sharpless, Angew. Chem., Int. Ed., 2001, 40, 2004; (b) C. Barner-Kowollik, F. E. Du Prez, P. Espeel, C. J. Hawker, T. Junkers, H. Schlaad and W. Van Camp, Angew. Chem., Int. Ed., 2011, 50, 60; (c) R. K. Iha, K. L. Wooley, A. M. Nystrom, D. J. Burke, M. J. Kade and C. J. Hawker, Chem. Rev., 2009, 109, 5620; (d) B. S. Sumerlin and A. P. Vogt, Macromolecules, 2010, 43, 1.
- 5 For example, see: (*a*) V. V. Rostovtsev, L. G. Green, V. V. Fokin and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2002, **41**, 2596; (*b*) J. A. Opsteen and J. C. M. van Hest, *Chem. Commun.*, 2005, 57.
- 6 (a) D. R. Wang, G. Ye, X. L. Wang and X. G. Wang, Adv. Mater., 2011, 23, 1122; (b) D. R. Wang, G. Ye, Y. Zhu and X. G. Wang, Macromolecules, 2009, 42, 2651; (c) P. C. Che, Y. N. He and X. G. Wang, Macromolecules, 2005, 38, 8657; (d) H. P. Wang, Y. N. He, X. L. Tuo and X. G. Wang, Macromolecules, 2004, 37, 135; (e) Y. N. He, X. G. Wang and Q. X. Zhou, Polymer, 2002, 43, 7325; (f) X. G. Wang, J. Kumar, S. K. Tripathy, L. Li, J. Chen and S. Marturunkakul, Macromolecules, 1997, 30, 219.