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Unimolecular Nanoparticles *via* Carbon-Carbon “Click” Chemistry for All-Polymer Nanocomposites

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Summary: We report for the first time the synthesis of unimolecular polystyrene-based nanoparticles (PS-NPs) under normal air atmosphere by direct carbon-carbon “click” chemistry (*i.e.*, “self-click” chemistry). First, statistical poly(styrene-*co*-4-vinylbenzyl chloride) copolymers synthesized by RAFT polymerization were decorated in a facile manner with alkyne groups by reaction with potassium propiolate, providing well-defined nanoparticle precursors (PS-Prec). Next, individual PS-Prec chains were collapsed irreversibly to unimolecular nanoparticles of *ca.* 12 nm in size by intrachain Cu(II)-catalyzed alkyne dimerization under high-dilution conditions, as revealed by SEC, H^1-NMR, DLS and TEM measurements. Based on predictions from a recent compressible thermodynamic model, the resulting nanoparticles could be promising materials for the development of homogeneous, miscible PS-NPs / polycarbonate all-polymer nanocomposites.

Keywords: blends; miscibility; nanocomposites; nanoparticles

Introduction

Unimolecular polymeric nanoparticles (NPs), also called single-chain-NPs or soft-NPs, are emerging nano-objects displaying dimensions below 20 nm showing interesting properties for different end-use applications: processing additives,[1] blend compatibilizers,[2] artificial enzymes[3] photostable bio-imaging agents,[4] or drug/siRNA-delivery systems.[5] In recent years, several routes to unimolecular nanoparticles have been pursued relying on efficient synthetic methods for the controlled, irreversible intramolecular collapse of individual polymer chains. In this sense, different synthetic approaches have been reported: from free-radical cross-linking of vinyl units,[6–8] to thermal cross-linking of benzocyclobutene and o-quinodimethane functional groups by Diels-Alder reactions,[9,10] to fast cross-linking of isocyanate groups from appropriate precursor chains by *diamines*.[11]

In an attempt to solve most of the severe limitations of the above techniques, we introduced the macromolecular “click” cycloaddition route[12–14] which relies in the use of alkyne and azide functional groups allowing the r.t. synthesis of unimolecular NPs by copper-catalyzed azide-alkyne “click” chemistry (i.e., nitrogen-carbon (N-C) “click” chemistry). However, the lack of a facile single-chain nanoparticle synthesis route *via* highly-efficient carbon-carbon (C–C) “click” chemistry has persisted.

In this work, we report for the first time the synthesis of polystyrene-based nanoparticles (PS-NPs) of *ca.* 12 nm in size by direct C–C “click” chemistry under normal air atmosphere starting from well-defined nanoparticle precursors containing alkyne functional groups. The intrachain collapsed PS-NPs were characterized by a combination of techniques including SEC, ^{1}H-NMR spectroscopy, DLS and TEM. Interestingly,

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based on the predictions of a recent compressible thermodynamic model, the resulting nanoparticles could be promising materials for the development of homogeneous, miscible PS-NP/polycarbonate all-polymer nanocomposites.

Experimental Part

Materials

Styrene (S) ($\geq$99.0%), 4-vinylbenzyl chloride (VBC) (90%), azobis(isobutyronitrile) (AIBN) (98%), propiolic acid (PA) (95%), potassium hydroxide (KOH) (90%), tetrabutyl ammonium bromide (TBAB) ($\geq$98.0%), copper(II) chloride ($CuCl_2$) ($\geq$99.995% trace metals basis), triethylamine (Et_3N) ($\geq$99.0%), and deuterated chloroform ($CDCl_3$) (99.96 atom % D, containing 0.03% (v/v) tetramethylsilane, TMS) were purchased from Aldrich and used, unless specified, as received. Toluene (HPLC grade), methanol (synthesis grade), tetrahydrofuran (THF) (HPLC grade), and N,N-dimethyl formamide (DMF) (synthesis grade) were purchased from Scharlab. S-(2-cyano-2-propyl)-S-dodecyltrithio-carbonate (CDT), (>97%) was purchased from Strem Chemicals. S and VBC were purified by passing through neutral alumina.

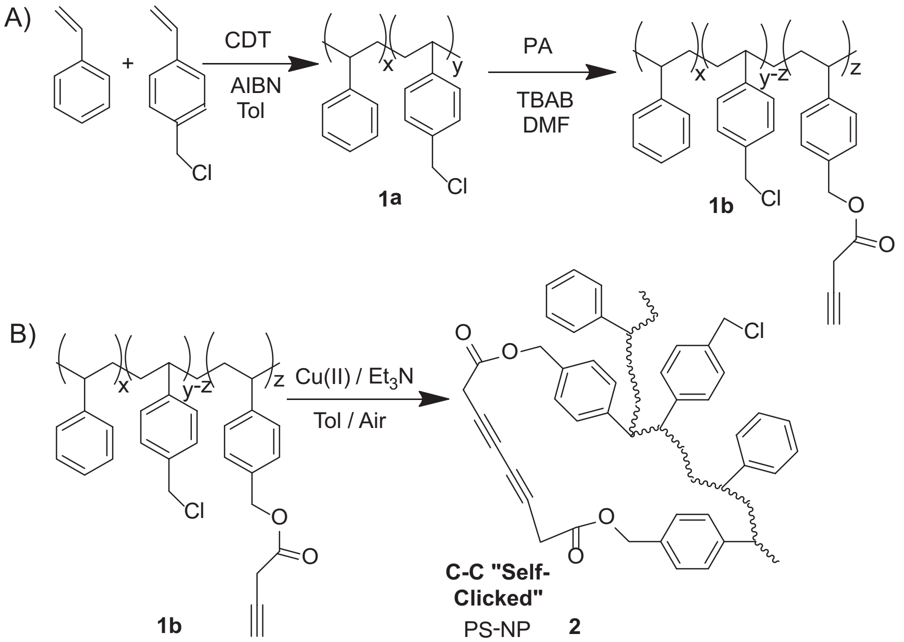
Characterization

^{1}H-NMR spectra were recorded at room temperature on a Bruker spectrometer operating at 300 MHz using $CDCl_3$ as solvent. SEC measurements were performed at 30 °C on an Agilent 1200 system equipped with PLgel 5 μm Guard and PLgel 5 μm MIXED-C columns, a differential refractive index detector (Optilab Rex, Wyatt) and a multi-angle laser light scattering detector (Minidawn Treos, Wyatt). THF was used as eluent at a flow rate of 1 mL/min. IR spectra were acquired in a Jasco 6300 FTIR spectrometer. Hydrodynamic radius measurements were performed on a Malvern Zetasizer Nano ZS apparatus. TEM pictures were recorded on a 200 kV TECNAI G2 20 TWIN microscope.

Results and Discussion

Synthesis of uniform-in-size unimolecular nanoparticles by covalent intrachain cross-linking depends on the use of linear precursors of narrow molecular weight dispersity showing high intrachain reactivity under appropriate reaction conditions.[14] As schematically depicted in Scheme 1, "self-clicked" intrachain crosslinked PS nanoparticles (PS-NPs, **2**) can be prepared in a easy manner from alkyne-decorated PS precursors (PS Prec, **1b**) via intramolecular copper-catalyzed carbon-carbon coupling (Glaser-Hay coupling[15]). In this sense, a series of well-defined statistical copolymers containing S and VBC units, P(S-co-VBC), with low molecular weight dispersity (*e.g.*, **1a**: $M_w = 53.2$ kDa, $M_w/M_n = 1.18$, VBC content (^{1}H-NMR) = 31 mol%) were synthesized by RAFT polymerization at 65 °C using AIBN as initiator, CDT as chain transfer agent and by working up to a maximum fractional conversion of $c \approx 0.4$. P(S-*co*-VBC) copolymers were decorated with alkyne groups by reaction with potassium propiolate in DMF in the presence of TBAB (see Scheme 1) providing poly(styrene-co-4-vinylbenzyl chloride-co-4-vinylbenzyl propiolate), P(S-co-VBC-co-VBP), nanoparticle precursors (PS-Prec) of narrow molecular weight dispersity (*e.g.*, **1b**: $M_w = 57.1$ kDa, $M_w/M_n = 1.18$, VBP content (^{1}H-NMR) = 19 mol%).

To guarantee individual nanoparticle formation through irreversible intrachain crosslinking of **1b**, the C–C "click" reaction was conducted under high-dilution conditions, at 0.1 mg **1b**/mL. Nanoparticle synthesis was performed in toluene under an atmosphere of normal air at 60 °C by using catalytic amounts of $CuCl_2$ (3 mol%) and Et_3N (3 mol%). Under such conditions, phenylacetylene as a reference provide the 1,3-diyne product in 6 h with excellent yield (99%).[16] The irreversible chain collapse accompanying nanoparticle formation was confirmed by SEC. As illustrated in Figure 1, a significant increase in SEC retention time (t_R) and, hence, a large reduction in hydrodynamic size ($D_H \propto t_R^{-1}$)



Scheme 1.
Illustration of A) synthesis of polystyrene-nanoparticle (PS-NP) precursor **1b**, and B) unimolecular nanoparticle construction from **1b** under normal air atmosphere through C-C "click" chemistry (Glaser-Hay coupling).

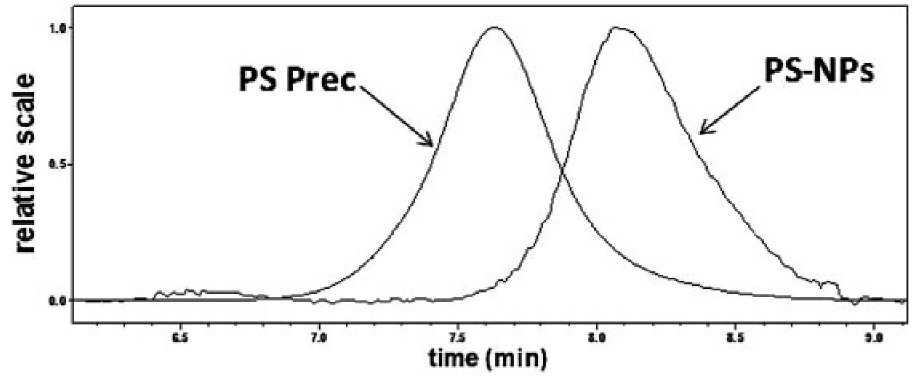


Figure 1.
SEC chromatograms of **1b** (PS Prec) and **2** (PS-NPs).

was observed for the collapsed PS-NPs **2** when compared to the PS Prec **1b**. Upon drying, **2** was found to be soluble in common organic solvents such as THF, chloroform and DMF. The average hydrodynamic size of **2** was 11 ± 2 nm, as determined by DLS.

Upon intrachain crosslinking of **1b**, a clear broadening in all ^{1}H-NMR signals was observed which was accompanied by a decrease in the relative intensity of some bands (data not shown). Two effects were responsible for this behavior: i) intramolecular crosslinking, and ii) insolubilization of

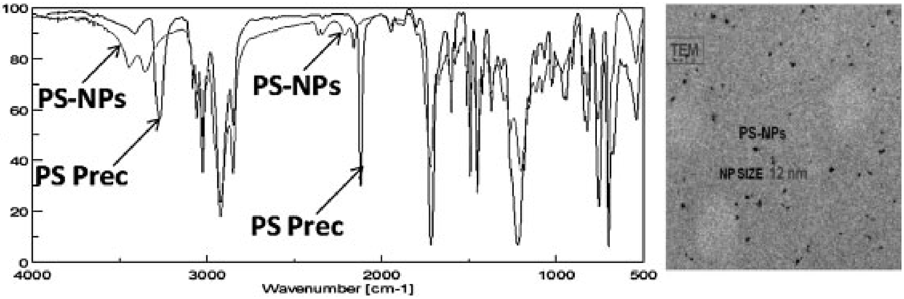


Figure 2.
FTIR spectra of **1b** (PS Prec) and **2** (PS-NPs) (left) and TEM picture of PS-NPs **2** (right).

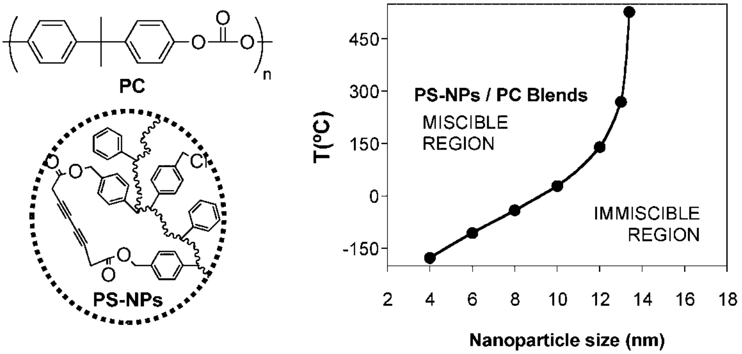


Figure 3.
Phase diagram of PS-NPs/PC blends, as predicted by a compressible model for weakly interacting all-polymer nanocomposites.[17] The volume fraction of PS-NPs in the blend was 20%.

a fraction of groups, those placed at the inner part of the single-chain nanoparticle. Based on the residual intensity of the IR vibration band corresponding to the $\equiv$C–H group at 2155 cm^{-1} (see Figure 2, left), the degree of alkyne homocoupling in **2** was estimated to be >95%. PS-NPs of *ca.* 12 nm in size were clearly observed by TEM (see Figure 2, right) in excellent agreement with DLS results.

Finally, predictions about the phase diagram of PS-NPs / polycarbonate (PC) all-polymer nanocomposites as a function of PS-NP size are provided in Figure 3, based on calculations from a compressible model introduced by Ruiz de Luzuriaga *et al.*[17] Interestingly, total miscibility (homogeneity) from r.t. to high temperatures is expected for PS-NPs showing a diameter < 10 nm.

Conclusion

Successful synthesis of well-defined P(S-*co*-VBC-*co*-VBP) nanoparticle precursors *via* RAFT polymerization followed by easy alkyne functionalization has been demonstrated. The versatility of the "self-clickable" *precursors* has allowed for the first time the facile and highly-efficient preparation under normal air atmosphere of uniform PS-NPs through intrachain C-C "click" chemistry. The resulting PS-NPs are predicted to form miscible, homogeneous bends with PC chains at nanoparticle size < 10 nm.

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[1] A. Tuteja, P. M. Duxbury, M. E. Mackay, *Macromolecules* **2007**, *40*, 9427.

[2] J. A. Pomposo, A. Ruiz de Luzuriaga, I. García, A. Etxeberria, J. Colmenero, *Macromol. Rapid Commun.* **2011**, *32*, 573.

[3] G. Wulff, B.-O. Chong, U. Kolb, *Angew. Chem. Int. Ed.* **2006**, *45*, 2955.

[4] C. T. Adkins, H. Muchalski, E. Harth, *Macromolecules* **2009**, *42*, 5786.

[5] A. Tamura, Y. Nagasaki, *Nanomedicine* **2010**, *5*, 1089.

[6] D. Mecerreyes, V. Lee, C. J. Hawker, J. L. Hedrick, A. Wursch, W. Volksen, T. Magbitang, E. Huang, R. D. Miller, *Adv. Mater.* **2001**, *13*, 204.

[7] K. S. Park, D. Y. Kim, S. K. Choi, D. H. Suh, *Jpn. J. Appl. Phys.* **2003**, *42*, 3877.

[8] J. Jiang, S. Thayumanavan, *Macromolecules* **2005**, *38*, 5886.

[9] E. Harth, B. V. Horn, V. Y. Lee, D. S. Germack, C. P. Gonzales, R. D. Miller, C. J. Hawker, *J. Am. Chem. Soc.* **2002**, *124*, 8653.

[10] T. A. Croce, S. K. Hamilton, M. L. Chen, H. Muchalski, E. Harth, *Macromolecules* **2007**, *40*, 6028.

[11] J. B. Beck, K. L. Killops, T. Kang, K. Sivanandan, A. Bayles, M. E. Mackay, K. Wooley, C. J. Hawker, *Macromolecules* **2009**, *42*, 5629.

[12] L. Oria, R. Aguado, J. A. Pomposo, J. Colmenero, *Adv. Mater.* **2010**, *22*, 3038.

[13] A. Ruiz de Luzuriaga, I. Perez-Baena, S. Montes, I. Loinaz, I. Odriozola, I. Garcia, J. A. Pomposo, *Macromol. Symp.* **2010**, *296*, 303.

[14] A. Ruiz de Luzuriaga, N. Ormategui, H. J. Grande, I. Odriozola, J. A. Pomposo, I. Loinaz, *Macromol. Rapid Commun.* **2008**, *29*, 1156.

[15] C. J. Li, *Accounts Chem. Res.* **2010**, *43*, 581.

[16] D. Wang, J. Li, N. Li, T. Gao, S. Hou, B. Chen, *Green Chem.* **2010**, *12*, 45.

[17] A. Ruiz de Luzuriaga, H. J. Grande, J. A. Pomposo, *J. Chem. Phys.* **2009**, *130*, 84905.