



Synthesis and Characterization of Functional Polymer Nanoparticle via Sonogashira Coupling

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ABSTRACT

We present the synthesis of single-chain nanoparticles via a palladium catalyzed Sonogashira coupling reaction. Intra-chain cross-linking of various linear polymers was achieved using an external cross-linker. The resulting nanoparticles were characterized by using triple detection size exclusion chromatography (SEC) where MALS gives the absolute molecular weight and viscometric detector gives the particle size.¹ Particle size can be tuned through molecular weight and by degree of cross-linking.

SIGNIFICANCE

The synthesis of structurally well-defined polymer nanoparticles with a size of 5-20 nm has attracted attention over the past years. These functionalized nanomaterials have myriad of potential applications in the fields of drug-delivery, biomimetic system, chemosensors and molecular imaging. One approach, involves intra-chain cross-linking of linear polymer chains in to single-chain nanoparticles (SCNP) with a size smaller than the original solvated polymer coil (Figure 1).²

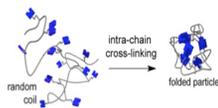


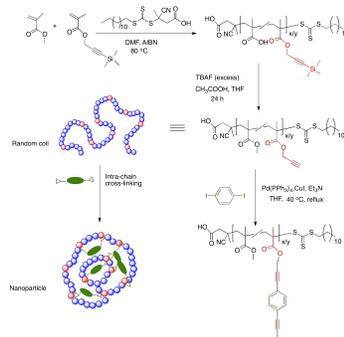
Figure 1: Single-chain polymer folding

Sonogashira coupling, a palladium catalyzed cross-coupling reaction, to form carbon-carbon bonds was first reported by Kenichi Sonogashira, Yosou Tohda, Hobue Hagihara.³ The high efficacy, selectivity, high yield, negligible side products and mild reaction conditions make the Sonogashira coupling reaction an efficient candidate for a macromolecular reaction.

In the present work, we introduce Sonogashira coupling as a mean for the synthesis of single-chain nanoparticles. The present route involves:
1) Synthesis of well-defined random copolymers containing trimethylsilyl protected alkyne groups distributed along the polymer chain. 2) Removal of the trimethylsilyl group to yield the corresponding terminal alkyne functionalized random copolymers. 3) Use of an appropriate bifunctional dihalide cross-linker and application of the Sonogashira coupling reaction conditions to an efficient intra-chain cross-linking.

MATERIALS AND METHODS

Poly(trimethylsilyl propargylmethacrylate-co-methylmethacrylate) with different chain lengths and varying amount of trimethylsilyl propargylmethacrylate were synthesized using RAFT polymerization. ¹HNMR spectroscopy was used to determine the composition of various linear polymers. Deprotection of these linear polymers using TBAF/CH₃COOH yielded corresponding alkyne functionalized copolymers. These linear polymer chains were cross-linked via 1,4-Diiodobenzene as a cross-linker (Scheme1).



Scheme1: Schematic illustration of synthesis of single chain nanoparticles

RESULTS

Initial attempts of the cross-linking reaction were performed on a parent polymer scaffold with a total final polymer concentration of ca 5 mg/ml in the reaction mixture. The resulting nanoparticles were characterized by triple detection SEC and the visual evidence for the particle formation was provided by transmission electron microscopy (TEM).

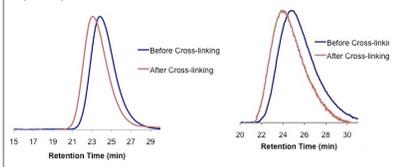


Figure 2: Normalized SEC Traces (THF, MALS, RI) (conc. 5mg/ml)

Concentration Dependant Studies

Further studies were carried out to study the effect of polymer concentration in the reaction mixture on the cross-linking phenomenon. The results of various experiments with final concentration of the reaction mixture are shown below. SEC data confirms nanoparticle formation via reduction in intrinsic viscosity (η) and viscometric radius (R_{η}).

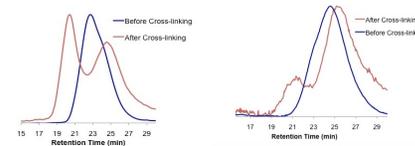


Figure 3: Normalized SEC Traces (THF, MALS, RI) (conc. 2 mg/ml)

	Mw (Kg/mol)	% alkyne	η (ml/g)	R_{η} (nm)
Before	28	23	36.2	4.6
After	32		21.9	4.1

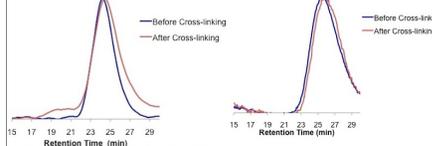


Figure 4: Normalized SEC Traces (THF, MALS, RI) (conc. 1 mg/ml)

	Mw (Kg/mol)	% alkyne	η (ml/g)	R_{η} (nm)
Before	28	10	9.5	3.6
After	33		6.0	3.3

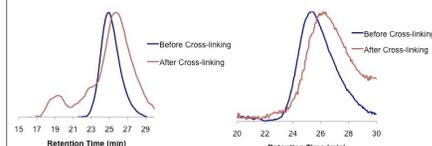


Figure 5: Normalized SEC Traces (THF, MALS, RI) (conc. 1mg/ml)

	Mw (Kg/mol)	% alkyne	η (ml/g)	R_{η} (nm)
Before	13	50	30.0	4.2
After	24		11.8	3.5

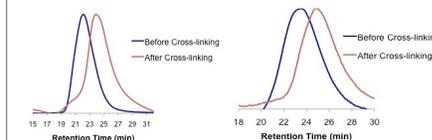


Figure 6: Normalized SEC Traces (THF, MALS, RI) (conc. 1 mg/ml)

	Mw (Kg/mol)	% alkyne	η (ml/g)	R_{η} (nm)
Before	55	40	57.2	7.1
After	43		21.3	5.3

Molecular Weight Dependent Studies

Alternatively, the cross-linking phenomenon was investigated for polymers with the same amount of alkyne functionality and different molecular weight. All SEC traces showed greater shift in retention time for a higher Mw polymer as compared to a low Mw polymer.

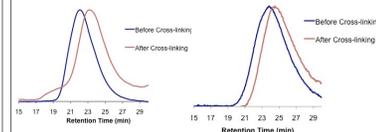


Figure 7: Normalized SEC Traces (THF, MALS, RI) of a High Mw polymer

	Mw (Kg/mol)	% alkyne	η (ml/g)	R_{η} (nm)
Before	61	30	38.0	8.1
After	51		30.8	6.1

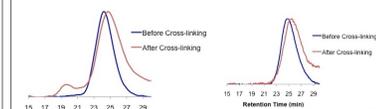


Figure 8: Normalized SEC Traces (THF, MALS, RI) of a low Mw polymer

	Mw (Kg/mol)	% alkyne	η (ml/g)	R_{η} (nm)
Before	37	30	14.7	4.2
After	39		11.5	4.0

CONCLUSIONS

We have shown that both inter and intra-chain cross-linked polymer nanoparticles can be synthesized via palladium catalyzed Sonogashira coupling. At a higher polymer concentration in the reaction mixture, inter-chain cross-linking predominated, while by decreasing the concentration intra-chain cross-linking was favored. We have also demonstrated that by changing the molar percent of alkyne, as well as molecular weight of the parent polymer, the size of resulting nanoparticle can be controlled.

References

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