

**Arm-Degradable Star Polymers with Crosslinked Ladder-Motif Cores as a Route to Soluble Microporous Nanoparticles**

Journal:	<i>Polymer Chemistry</i>
Manuscript ID	PY-COM-07-2019-001060.R1
Article Type:	Communication
Date Submitted by the Author:	18-Aug-2019
Complete List of Authors:	Teo, Yew Chin; Stanford University, chemistry Lai, Holden; Stanford University, Chemistry Xia, Yan; Stanford University, Chemistry

## COMMUNICATION

## Arm-Degradable Star Polymers with Crosslinked Ladder-Motif Cores as a Route to Soluble Microporous Nanoparticles

Received 00th January 20xx,  
Accepted 00th January 20xx

Yew Chin Teo, Holden W.H. Lai and Yan Xia\*

DOI: 10.1039/x0xx00000x

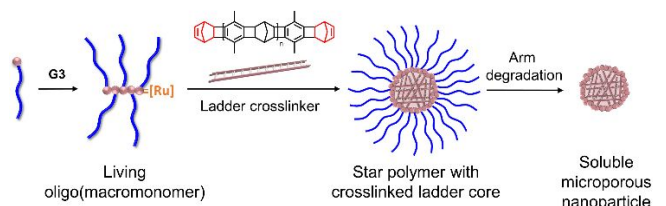
**We report a strategy to synthesize controlled star polymers with cores consisting of crosslinked (macro)molecular ladder motifs. In this strategy, living ROMP of norbornenes or norbornene-terminated macromonomers was used to produce arms followed by crosslinking using ladder-shaped dinorbornenes or norbornene-terminated ladder polymers to form star polymers. When degradable grafted arms were used, the cores can be isolated as soluble polymeric nanoparticles upon arm degradation. We demonstrated the presence of microporosity from the crosslinked ladder core of star polymers. This strategy provides access to a new class of soluble and stable microporous polymeric nanoparticles.**

Microporous polymers have become increasingly important for many applications, including gas storage, separation, and heterogeneous catalysis.<sup>1-3</sup> Many types of porous materials, such as conjugated microporous polymers (CMPs) and hyper-cross-linked polymers (HCPs), have been developed and exhibit large surface areas with high chemical and structural tunability.<sup>4-7</sup> However, the insolubility of such network materials poses processing challenges,<sup>8</sup> hampering their applications. Recently, soluble microporous organic materials, including porous organic cages (POCs)<sup>9, 10</sup> and polymers of intrinsic microporosity (PIMs),<sup>11, 12</sup> have attracted significant attention for their processing advantages in a range of applications.

Soluble crosslinked microporous polymers can possess both robust pore structures and the processability of soluble polymers, but such examples are very scarce in literature.<sup>13-15</sup> We imagined the access to such crosslinked microporous polymers via core-crosslinked star polymers that are synthesized via an arm-first approach followed by crosslinking with micropore-generating motifs. This core-shell type of star polymers consist of a heavily crosslinked core and many arm polymers that render solubility.<sup>16, 17</sup> If the arms can be further

degraded or cleaved, the core may be isolated as microporous polymer nanoparticles. Although very rare in literature, Sawamoto and coworkers have shown that arm-cleavable star polymers can give soluble microgels upon arm cleavage.<sup>18</sup>

With our interest in microporous polymers, our group has previously developed catalytic arene-norbornene annulation (CANAL) reaction between norbornadiene and dibromo-arenes to synthesize a family of structurally rigid ladder polymers that are microporous due to frustrated chain packing.<sup>19-22</sup> The exclusive stereoselectivity of CANAL reaction produces only 4-membered ring fused *exo*-norbornene (NBE), which is the favorable NBE configuration for fast ring-opening metathesis polymerization (ROMP). Therefore, we envisioned that rigid ladder-shaped diNBEs or even NBE-terminated telechelic ladder polymers from CANAL reaction may be effective crosslinkers for the synthesis of core-crosslinked star polymers via ROMP. The shape-persistent crosslinkers may give rise to a microporous core in the star polymers. Further, degrading the arms may lead to soluble cores as microporous polymer nanoparticles (Scheme 1). Although the synthesis of core-crosslinked star polymers has been extensively investigated using controlled radical polymerizations,<sup>16, 17, 23</sup> their synthesis via ROMP has been much less explored. Schrock and Nomura groups reported the ROMP synthesis of star polymers with low dispersities via the arm-first approach using diNBEs as the crosslinkers.<sup>24-26</sup> Johnson and co-workers synthesized high molecular weight (MW) brush-arm star polymers with drugs loaded in the cores and demonstrated their applications in drug delivery.<sup>27-30</sup>

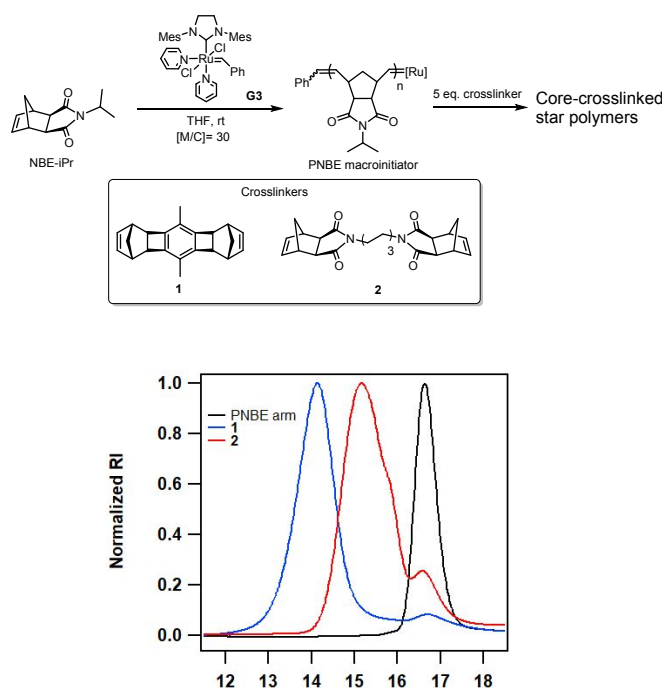


**Scheme 1** Design of star polymers with degradable oligo-macromonomer arms and a core crosslinked by (macro)molecular ladders, which give soluble microporous microgels after degradation of arms.

\*Department of Chemistry, Stanford University, Stanford, California 94305, United States. Email: yanx@stanford.edu

†Electronic Supplementary Information (ESI) available: Experimental procedures, NMR spectra, SEC traces, and sorption isotherms. See DOI: 10.1039/x0xx00000x

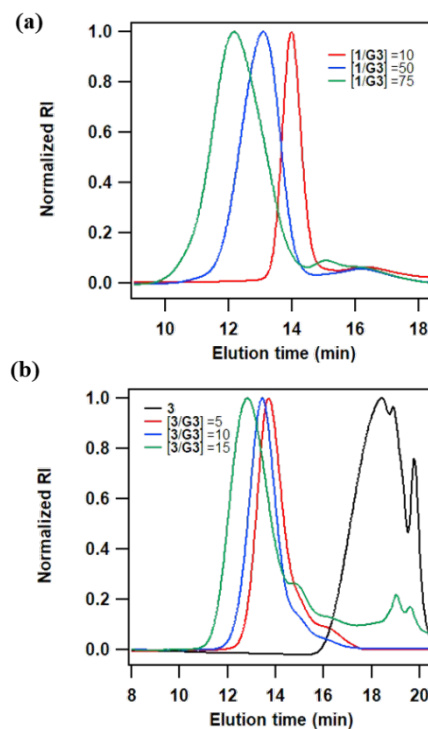
We set out to explore the use of ladder-shaped (macro)molecular motifs as crosslinkers to synthesize star polymers. We first synthesized a ladder-shaped diNBE **1** using CANAL between 2,5-dibromo-*p*-xylene and excess norbornadiene, and investigated the effectiveness of **1** as a crosslinker for the synthesis of star polymers via ROMP. 1 equiv of 3<sup>rd</sup> generation Grubbs catalyst (**G3**) was added to 30 equiv of a substituted NBE (NBE-*i*Pr) to form a macroinitiator with an average degree of polymerization (DP) of 30. After complete conversion of NBE-*i*Pr, 5 equiv of **1** was injected into the ROMP reaction. Within 1 h at room temperature, > 95% of the PNBE macroinitiator was converted to a relatively narrow-disperse star polymer with  $M_w = 430$  kDa and  $\mathcal{D} = 1.20$ . In contrast, using the same equivalence of a diNBE **2** with a flexible hexyl linker resulted in almost 10 times lower MW for the formed star polymer with clearly noticeable unreacted macroinitiator shown by GPC analysis (Figure 1). This comparison clearly indicated that the rigid ladder diNBE is indeed a very effective crosslinker to form star polymers via ROMP. While a flexible diNBE can potentially undergo metathesis of both NBE motifs at the same chain end, a rigid ladder diNBE prevents this possibility due to the rigid extended conformation, and promotes crosslinking with another reactive chain end and incorporates a larger number of arms into the formed star polymers. Notably, CANAL chemistry can produce a variety of rigid diNBEs to potentially function as effective crosslinkers for the synthesis of star polymers via ROMP.



**Fig. 1** Arm-first synthesis of core-crosslinked star polymers using ROMP of NBE-*i*Pr and diNBEs **1** and **2** as crosslinkers. Crude GPC traces of the PNBE macroinitiator (black) and star polymers crosslinked using **1** (blue) and **2** (red).

After the initial study to confirm effective core crosslinking using CANAL diNBE, we moved to designing star polymers with degradable arms. Using a degradable macromonomer (MM) to

prepare grafted arms would allow removal of the majority of the arm content after the star polymer synthesis. We first synthesized a NBE-terminated poly(lactide) (PLA) with  $M_n = 5.0$  kDa as the MM using the previously reported method.<sup>31</sup> 1 equiv of **G3** was added to 5 equiv of PLA MM to form a short living oligoMM with an average DP of 5. Upon complete consumption of PLA MM within 5 min, different amounts of **1** (10, 50, 75, and 100 equiv relative to **G3**) were added and the reactions were allowed to proceed for 3 h. High conversions (> 90%) of oligoMM to soluble star polymers **S1-S3** (Table 1) were achieved for all the crosslinker loadings except for 100 equiv of **1**, which resulted in gelation. GPC analysis of the crude star polymers showed monomodal MW distribution with  $\mathcal{D} = 1.1$ -1.3 and  $M_w$  increased from 160 to 1820 kDa with increasing the equivalence of added crosslinker from 10 to 75 (Figure 2a and Table 1). Using multi-angle laser light scattering (MALLS), we determined the absolute MWs of the star polymers, which were used to calculate the average number of arms (in our case, the number of oligoMMs) to be 6, 15, and 36 for 10, 50, and 75 equiv (relative to initiator **G3**) of crosslinker **1** (Table 1, entry 1-3). <sup>1</sup>H NMR spectroscopy of the resulting star polymer showed resonances predominantly from the PLA arms, while signals expected from the crosslinked ladder core were almost invisible (Figure S7a), which is reasonable given the reduced segmental mobility of the core.



**Fig. 2** GPC traces of crude star polymers with oligomacromonomer (PLA) arms and crosslinked cores by (a) ladder diNBE **1** and (b) NBE-terminated ladder polymer **3** at different loadings of crosslinkers. The black trace in (b) is the NBE-terminated ladder polymer **3**.

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**Table 1** Synthesis of core-crosslinked star polymers with oligomacromonomer arms<sup>[a]</sup>

entry	star polymer	crosslinker (XL)	[XL/G3]	conv. (%) <sup>[b]</sup>	$N_{\text{arm}}$ <sup>[c]</sup>	$M_{w,\text{MALLS}}$ (kDa) <sup>[d]</sup>	$\bar{D}_M$ <sup>[d]</sup>	$D_h$ (nm) <sup>[e]</sup>	weight % of core
1	<b>S1</b>	<b>1</b>	10	95	6	160	1.14	14.2	11
2	<b>S2</b>	<b>1</b>	50	95	15	600	1.30	23.9	38
3	<b>S3</b>	<b>1</b>	75	>90	36	1820	1.30	26.0	50
4	<b>S4</b>	<b>1</b>	100	gel	-	-	-	-	-
5	<b>S5</b>	<b>3</b>	5	>95	10	331	1.37	22.0	30
6	<b>S6</b>	<b>3</b>	10	>95	21	913	1.35	22.5	44
7	<b>S7</b>	<b>3</b>	15	>90	50	2968	1.22	28.0	55

[a] Conditions:  $[\text{PLA oligoMM}]_0 = 0.30$  mM in THF at room temperature. [b] Conversion of PLA oligoMM to star polymer, estimated by comparing the peak areas of star polymer and residual oligoMM from GPC traces of the crude product. [c] Number of oligoMM arms per star:  $N_{\text{arm}} = (\text{weight fraction of arms}) \times M_{w,\text{star,MALLS}} / M_{w,\text{oligoMM arm}}$ . [d] Determined by GPC in THF using RI and MALLS detectors. [e] Hydrodynamic diameter of the star polymers determined by DLS in THF.

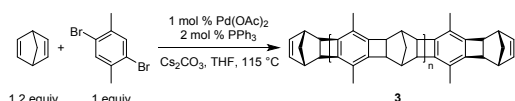
Encouraged by the results using small molecule ladder-shaped diNBE crosslinker, we next explored the possibility of using NBE-terminated ladder polymers as the macromolecular crosslinker in the star polymer synthesis. CANAL polymerization between norbornadiene and aryl dibromides is presumably a step-growth polycondensation, so we synthesized a simple NBE-terminated ladder polymer **3** using norbornadiene in 20 mol% excess to *p*-dibromo-*p*-xylene to ensure end-capping of the ladder polymer with NBE motifs (Scheme 2).  $^1\text{H}$  NMR spectroscopy of the isolated ladder polymer clearly showed signals from the NBE olefin protons, and the integration ratio of NBE signals to the ladder backbone signals corresponds to approximately 10 repeat units and a MW of about 2 kDa (Figure S6). Similar to the synthetic procedure of star polymers using **1**, living PLA oligoMM with an average DP = 5 was added to 5, 10, and 15 equiv of **3** relative to **G3**. Delightfully, > 90% conversion of oligoMM was achieved in all cases to yield soluble star polymers **S5–S7** with  $M_w$  dramatically increasing from 330 to nearly 3000 kDa with increasing the equivalence of ladder polymer crosslinker from 5 to 15 (Figure 2b and Table 1, entry 5–7). When 5 or 10 equiv of **3** was used, we also observed complete incorporation of **3** as evident from the complete disappearance of the peaks corresponding to **3** in GPC traces (Figure 2b).  $^1\text{H}$  NMR spectroscopy of the resulting star polymer showed strong

signals from the PLA arms as well as some signals from the core of crosslinked ladder polymer, albeit strongly suppressed as compared to the signals from the arms (Figure S8a).

The grafted PLA arms of the star polymers were subsequently degraded using 4 M HCl in dioxane in the presence of a trace amount of water at 80 °C. The remaining crosslinked cores were isolated via precipitation into methanol. Notably, the surfaces of these star polymer cores after PLA degradation are presumably dangled with very short oligoNBE appending hexanol groups, because this was the backbone of oligoMM arms. Potentially, these oligoNBE surface groups can be used to functionalize the surface of the core particles in the future. Interestingly, after the arm degradation, most of the isolated cores consisting of crosslinked diNBE or ladder polymers remained soluble in nonpolar organic solvents, such as THF and DCM. Complete hydrolysis of arms was confirmed by the absence of any signals from PLA in the NMR spectroscopy of isolated cores. The higher MW star polymers that contained the highest fraction of core, **S3** and **S7**, resulted in a cloudy insoluble suspension upon hydrolysis of grafted arms, suggesting that the larger size of cores was difficult to be solubilized after removal of arms.  $^1\text{H}$  NMR spectroscopy of the arm-degraded cores showed broad peaks expected from the crosslinkers with suppressed intensity. While no remaining NBE olefin signal could be seen

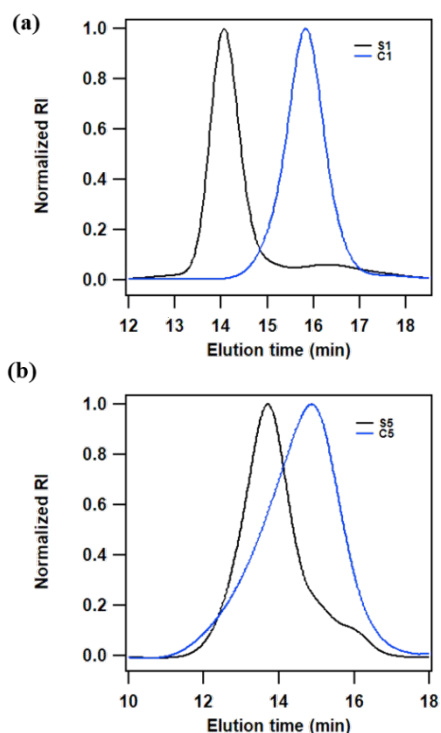
for arm-degraded core of **S2** with small molecular diNBE (Figure S7b), a noticeable NBE olefin peak was observed for arm-degraded core of **S5** from unreacted terminal NBE on ladder polymer crosslinker buried in the core (Figure S8b).

We characterized the soluble isolated cores from **S1-2** and **S5-6**, which were crosslinked by small molecular and polymeric ladders **1** and **3** respectively, using dynamic light scattering (DLS) and GPC. As expected, we observed a reduction in the hydrodynamic diameter ( $D_h$ ) from the parent star polymers to the arm-removed cores based on DLS measurements. For example,  $D_h$  of **S1** and **S5** decreased from 14.2 and 22.0 nm to 6.6 and 15.3 nm after arm degradation, respectively. GPC analysis also showed a clear shift to the longer elution times



**Scheme 2** Synthesis of NBE-terminated ladder polymer **3** via CANAL polymerization.

for the isolated cores as compared to their parent star polymers, corresponding to  $M_w = 44$  and 520 kDa for cores from **S1** and **S5**, respectively (Figure 3). For the isolated core of



**S5**, its higher measured  $M_w$  than that of **S5** is due to aggregation of the core as evidenced by its asymmetric GPC trace. For star polymers with a larger fraction of core, **S2** and **S6**, a high molecular weight shoulder was clearly observed in the GPC trace of the core (Figure S1), suggesting microscopic aggregation.

**Fig. 3** GPC traces of star polymers (**S**, black traces) and their corresponding cores after arm degradation (**C**, blue traces) for (a) **S1** and (b) **S5**.

We have previously observed high surface areas and microporosity from the CANAL ladder polymers,<sup>19-21</sup> and we suspected the presence of microporosity in the crosslinked ladder polymers or even the small molecule ladder diNBE. Therefore, we measured the Brunauer-Emmett-Teller (BET) surface area of the isolated dried solid of cores (Figure S2-3). Using CO<sub>2</sub> sorption at 195 K, we measured the cores isolated from **S2** and **S6** to have high BET surface areas of 213 and 504 m<sup>2</sup>/g, respectively. The relatively high surface area in the isolated cores suggested the retention of microporosity in the crosslinked molecular ladders, even in crosslinked ladder small molecules. The much higher surface area of crosslinked ladder polymer core than the small molecule core suggested more frustrated chain packing inside the ladder polymer core.

In summary, we report the synthesis of star polymers with microporous cores using ROMP. The cores were heavily crosslinked by ladder diNBE or NBE-terminated ladder polymers that were easily synthesized via CANAL. Soluble microporous cores can be obtained upon arm degradation. This synthetic approach of using sacrificial star polymers with crosslinked rigid cores gives access to soluble microporous polymer nanoparticles, which may be used for separation applications with processing advantages and as filler components for mixed matrix membranes or other materials. This strategy can be generalized to different sacrificial grafted arms and different rigid diNBES to form crosslinked cores with the chemical and structural tunability.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

We thank U.S. Army Research Office (W911NF-16-1-0018) to support this research. Y.X. thanks National Science Foundation for a CAREER award (CHE-1553780). Y.C.T was supported by an A\*STAR graduate fellowship. H.W.H.L. is supported by a NSF Graduate Research Fellowship (DGE- 156518).

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## TOC Entry

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Star polymers were synthesized via cores crosslinking of (macro)molecular ladder motifs and converted to microporous polymer particles after arm degradation

