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Expedient synthesis and ring-opening metathesis polymerization of pyridinonorbornenes†

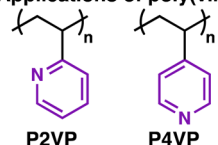
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Pyridine-containing polymers are promising materials for a variety of applications from the capture of contaminants to the self-assembly of block copolymers. However, the innate Lewis basicity of the pyridine motif often hampers living polymerization catalyzed by transition-metal complexes. Herein, we report the expedient synthesis of pyridinonorbornene monomers via a [4 + 2] cycloaddition between 2,3-pyridynes and cyclopentadiene. Well-controlled ring-opening metathesis polymerization was enabled by careful structural design of the monomer. Polypyridinonorbornenes exhibited high T_g and T_d , a promising feature for high-temperature applications. Investigation of the polymerization kinetics and of the reactivity of the chain ends shed light on the influence of nitrogen coordination on the chain-growth mechanism.

Pyridine-containing polymers offer a wealth of applications stemming from their unique electronic features and the Lewis and Brønsted basicity of the nitrogen atom (Fig. 1a).^{1,2} Yet, few pyridine-containing monomers have been exploited in controlled polymerizations, in part due to the coordinative ability of pyridine toward transition-metal catalysts. 2- and 4-Vinyl pyridines (2VP and 4VP) remain the rare examples of monomers that allow for the precise synthesis of soft materials containing pyridine in the main chain (Fig. 1a).^{1–3} Poly(vinyl pyridine)s (P2VP or P4VP) have been investigated for the removal of organic contaminants from wastewater,⁴ for metal absorption,¹ and as support for recyclable reagents in oxidation, reduction, or halogenation reactions.^{1,2} Vinyl pyridines have also emerged as monomers of choice for the self-assembly of

diblock copolymers.³ Finally, nitrogen quaternization provides a practical entry into polyelectrolytes.^{5,6} Interestingly, despite the well-documented functional-group tolerance of ring-opening metathesis polymerization (ROMP),^{7–9} the rare pyridine-containing ROMP monomers reported in the literature (M1–M3) do not undergo well controlled polymerizations (Fig. 1b).^{10–13} Coordinating monomers are indeed known to detrimentally affect the rates of initiation and propagation through chelation to the Ru catalyst.^{14–18} This issue is especially prevalent with monomers containing an unprotected amine in close proximity to the strained alkene.^{19–21}

(a) Applications of poly(vinyl pyridine)s



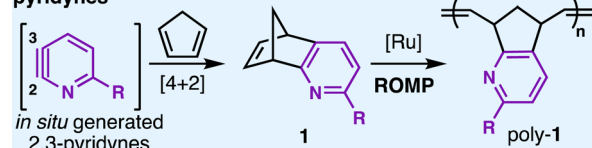
- Polydentate ligands
- Supported-reagent platform
- Copolymer self-assembly
- Polyelectrolyte precursors

(b) Prior pyridine-containing norbornyl monomers



- Poor or no control over ROMP likely due to N/Metal coordination

(c) This work: ROMP of pyridinonorbornenes derived from 2,3-pyridynes



- Expedient monomer synthesis
- Stable, derivatizable monomers
- Excellent control over M_n and chain-end fidelity
- High T_g and T_d

Fig. 1 (a) Poly(vinyl pyridine)s and some of their applications. (b) Prior examples of pyridine-containing norbornyl monomers. (c) Synthesis and ROMP of pyridinonorbornenes.

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Herein, we report the streamlined synthesis of a family of pyridinonorbornene monomers as analogs of 2VP for ROMP through the intermediacy of 2,3-pyridynes (Fig. 1c). Optimization of the monomer structure and ROMP conditions allowed the synthesis of pyridine-containing polymers with predictable molar masses, functionalizable chain ends, as well as high thermal stability and glass-transition temperature (T_g), a desirable feature for a number of high-temperature applications.^{22,23}

While pyridine motifs have been successfully incorporated into the backbone of macromolecules *via* polycondensation,^{24–27} very few controlled chain-growth polymerizations have been reported outside of PVPs. Buchmeiser and coworkers synthesized dipyridyl norbornene **M1** that was polymerized *via* ROMP with relatively high dispersity (D) values (1.6–1.8) using a Mo-based Schrock catalyst (Fig. 1b).^{10,11} Wakatsuki and coworkers subsequently polymerized monopyridyl norbornene **M2** using Grubbs 2nd generation Ru catalyst in a non-controlled fashion.¹² In both cases, coordination of the pyridine nitrogen to the metal alkylidene was postulated to be a main factor in the lack of control over molar mass distribution. Similarly, Iacono and coworkers recently reported the uncontrolled ROMP of monomers **M3**.¹³ However, the development of the 3rd generation of Grubbs catalysts that contains two pyridine ligands (typically 3-bromopyridine)²⁸ suggests that pyridine coordination is not necessarily detrimental to the ROMP process. Pyridine ligands have been shown to undergo a rapid association/dissociation equilibrium,²⁹ and Guironnet and coworkers recently demonstrated that the rate of polymerization is directly tied with their coordination strength.³⁰ We hypothesized that a fusion of the pyridine core to the norbornene as depicted in **1** would both increase the steric hindrance around the nitrogen and decrease the conformational freedom and flexibility of the pyridine core, thereby disfavoring coordination to the Ru center (Fig. 1c). Additionally, the introduction of a variety of R groups at the C6 position of **1** would provide a practical handle to further increase the steric bulk around the nitrogen and to concomitantly increase solubility of the targeted polymers in organic solvents.³¹

While pyridinonorbornenes **1** have never been reported as ROMP monomers, **1a** has been previously synthesized by Tanida and Irie in 14 steps and 2.7% overall yield from norbornadiene.³² Since this synthetic route would be hardly amenable to a scalable production of polymers and would create a bottleneck for the diversification of the monomer structure, a streamlined alternative was targeted. Inspired by the synthesis of benzonorbornene monomers *via* a Diels–Alder reaction between cyclopentadiene and benzyne reported by Feast³³ and subsequently by Maynard and Garg,³⁴ we hypothesized that utilizing a 2,3-pyridyne^{35–37} as the dienophile would provide an expedient and modular sequence toward the family of monomers **1a–c** (Fig. 2). Heterocyclic arynes such as 2,3-pyridynes have seen a resurgence in total syntheses of natural products^{38–40} but remain largely absent from the field of polymer synthesis. Following a procedure by Carrol,⁴¹ commercially available and inexpensive pyridone **2a** was converted to



Fig. 2 Synthesis of pyridinonorbornenes **1a–c** *via* 2,3-pyridynes. Reagents and conditions: (1) LDA (2.2 equiv.), THF, 0 °C, 1 h, then TMSCl (1.2 equiv.), 0 °C, 15 min, then rt, 12 h. (2) Tf₂O (1.1 equiv.), pyridine, 0 °C, 20 min, then rt, 12 h. (3) CsF (5.0 equiv.), C₅H₆ (5.0 equiv.), MeCN, 30 °C, 3 h. ^a4 : 1 MeCN : DCM.

3a in 62% yield *via* silylation and triflation. After optimization, it was found that upon *in situ* generation of 2,3-pyridyne using CsF, [4 + 2] cycloaddition with cyclopentadiene delivered pyridinonorbornene **1a** in 45% yield (28% yield from **2a**). When the same sequence was applied to hexyl variant **2b**, a drastic decrease in yield was observed in the preparation of **3b** caused by competitive silylation of the benzylic-like methylene in the hexyl chain. This finding prompted us to synthesize *tert*-butyl congener **2c** through a known two-step route.⁴² To our delight, **2c** could be converted to pyridyne precursor **3c** in a much improved 85% yield over two steps, and the following cycloaddition step provided **1c** in 55% yield resulting in a 47% overall yield from **2c**. The ring strain of pyridinonorbornenes **1a–c** was estimated *via* an isodesmic analysis of the opening of **1a–c** with ethylene.⁴³ The computed ring strain of each potential monomer was found to be higher than that of norbornene by ~7 kcal mol⁻¹ (ESI[†]), which indicated that ROMP of **1a–c** should be thermodynamically favorable. Unfortunately, initial polymerization attempts using monomer **1a** and Grubbs 3rd generation catalyst (**Ru-1**) resulted in virtually no conversion of monomer (Table 1, entry 1). Switching to hexyl monomer **1b** afforded similar results at room temperature but increasing the temperature to 60 °C led to a polymer with relatively low D and a M_n reasonably close to the predicted value, albeit with low monomer conversion (48% after 8 h; entries 2 and 3). Following this encouraging result, the polymerization of *tert*-butyl monomer **1c** was attempted. Gratifyingly, full monomer conversion could be reached in 5 h at room temperature at a 50 : 1 ratio of **1c** : **Ru-1**. Poly-**1c** exhibited good solubility in organic solvents including THF, DCM, and chloroform. SEC analysis revealed a narrow D of 1.07 and an excellent match between the experimental M_n and the predicted value (9.7 *vs.* 10.1 kg mol⁻¹; entry 4). Polymerization with Grubbs 2nd generation catalyst (**Ru-2**) afforded poly-**1c** with a slightly broader dispersity (D = 1.21; entry 5).⁴⁴ Careful analysis of ¹H and ¹³C NMR spectra, in combination with HSQC, HMBC, and COSY

Table 1 ROMP of pyridinonornbornenes

Entry ^a	M	Ru	t (h)	Conv. (%)	M_n^{theo} (kg mol ⁻¹)	$M_n^{\text{exp } b}$ (kg mol ⁻¹)	D^b
1	1a	Ru-1	22	Trace	—	—	—
2	1b	Ru-1	22	16	—	—	—
3 ^c	1b	Ru-1	8	48	5.6	3.4	1.38
4	1c	Ru-1	5	>99	10.1	9.7	1.07
5	1c	Ru-2	5	>99	10.1	9.9	1.21

^a Monomer (M, 0.10 mmol) was polymerized by Ru catalysts (0.002 mmol) in DCE at rt. ^b M_n 's and D 's were determined by SEC (THF) using polystyrene standards (RI detection). ^c Reaction temperature = 60 °C.

experiments (Fig. 3a and S38–41[†]) suggests that poly-1c likely exhibits regio irregularities from concurrent head-to-head or head-to-tail pathways. Mixed tacticities and *cis/trans* olefin stereochemistry could also contribute to the complexity of the NMR spectra. MALDI-TOF analysis confirmed the mass of the



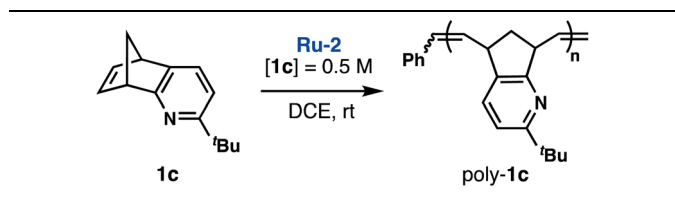
Fig. 3 (a) ¹H NMR spectrum of poly-1c in CDCl₃ (*). (b) MALDI-TOF analysis of poly-1c ($M_n^{\text{SEC}} = 5.0 \text{ kg mol}^{-1}$, $D = 1.12$).

repeating unit, as well as the installment of a methylene group at the chain end upon quenching with ethyl vinyl ether (EVE) (Fig. 3b).

In order to thoroughly characterize the livingness of the polymerization, the kinetics of the ROMP of 1c with Ru-1 were studied *via* ¹H NMR in CD₂Cl₂. The measured linear relation between $\ln([M_0]/[M_t])$ and time confirmed the first-order dependence in concentration of monomer 1c as expected for a living chain-growth process (Fig. 4a). The rate of polymerization of 1c with Ru-1 is notably lower than that of typical norbornene monomers.³⁰ M_n was found to grow linearly with conversion of 1c, and dispersity values remained below 1.2 throughout the ROMP (Fig. 4b). Of note, the quenching with EVE of the terminal Ru-carbene was noticeably slower with 1c when compared to more common ROMP monomers, which rendered accurate determination of the conversion of 1c over time challenging (Table S5[†]). Sequential addition of the strongly Lewis basic ligand 4-dimethylaminopyridine (DMAP)^{45,46} followed by EVE helped circumvent this issue. Poly-1c with higher degrees of polymerization were obtained by varying the ratio of monomer 1c to catalyst Ru-1, however a small shoulder was detected for DPs ≥ 100 corresponding to polymeric impurities roughly twice as large as the targeted M_n



Fig. 4 Polymerization of 1c with Ru-1 ([1c]:[Ru-1] = 50:1): (a) Determination of the rate of propagation ($R^2 = 0.998$) at 32 °C in CD₂Cl₂; (b) M_n (blue squares) and D (green triangles) vs conversion.

Table 2 ROMP of **1c** by Ru-2

Entry ^a	[1c]:[Ru]	<i>t</i> (h)	Conv. (%)	M_n^{theo} (kg mol ⁻¹)	$M_n^{\text{exp } b}$ (kg mol ⁻¹)	<i>D</i> ^b
1	100 : 1	11	85	17.0	16.7	1.17
2	200 : 1	25	90	36.0	29.7	1.12
3	300 : 1	37	93	55.7	49.8	1.11
4	400 : 1	42	87	69.4	77.6	1.12

^a **1c** (0.10 mmol) was polymerized with Ru-2 in DCE at rt for specified amounts of time. ^b M_n 's and *D*'s were determined by SEC (THF) using polystyrene standards (RI detection).

(Fig. S2a†). This shoulder was tentatively ascribed to adventitious cross metathesis between methylene and Ru-bond chain ends taking place during the slow quenching process. Fortunately, this issue was minimal with Ru-2, which afforded poly-**1c** with predictable M_n 's up to 77.6 kg mol⁻¹ (Table 2, entries 1–4; Fig. S2b†).

Chain-extension of poly-**1c** with additional **1c** provided evidence that the propagating chain ends are preserved after monomer depletion. Full conversion of **1c** was observed following the addition of a second batch of monomer concomitant with a uniform shift of the SEC trace (Fig. 5a). However, when chain extension was attempted with *exo*-norbornene diimide **4**, a bimodal distribution was observed clearly indicating partial chain extension (Fig. 5b top). Taken together with the relatively slow rates of polymerization and quenching with EVE, this finding suggests that the Lewis basic nitrogen of the terminal pyridine motif binds to the Ru center (Fig. 5b) thereby hampering reinitiation with a non- or poorly coordinating monomer such as **4**.^{14–18} A similar issue was encountered by Xia and coworkers in the synthesis of block copolymers containing a coordinating diester unit and solved through addition of 3-bromopyridine to facilitate the reinitiation.⁴⁷ This strategy allowed the isolation of poly-**1c-b-4** with minimal chain termination as shown by SEC and DOSY NMR (Fig. 5b bottom and S44†). Notably, the polymerization of the second block reached full conversion in about 1 h, while homopolymerization of **4** in the same conditions (catalyst, solvent, concentration, temperature, *etc.*) was complete in only a few minutes (Table S7†). The slow rate of propagation of **4** when used for chain extension likely indicates that nitrogens in the



Fig. 5 (a) Synthesis of poly-**1c**₁₀₀ via chain extension. (b) Synthesis of diblock copolymer poly-**1c-b-4** using 3-bromopyridine to facilitate reinitiation of the chain ends.

main chain of the poly-**1c** segment also coordinate to the catalyst. Random copolymerization of **1c** and **4** (~4:1) similarly led to a relatively slow polymerization of **4**. A simultaneous and almost quantitative incorporation of both monomers was observed over 10 h, while the molar mass distribution remained narrow and monomodal (Table S8† and Fig. S6†). These experiments point toward a dynamic and complex interplay between the Ru center and the Lewis basic nitrogens of the chain end, backbone, and monomer. Future work will investigate the influence of the coordination of each species over the ROMP process.

Lastly, the thermal properties of poly-**1c** were investigated. Due to the structural rigidity of its backbone, it was hypothesized that this material would possess a higher glass transition temperature than P2VP. Indeed, poly-**1c** exhibited a T_g of 157 °C *via* differential scanning calorimetry (DSC), which is significantly higher than the reported T_g of P2VP (~104 °C).^{3,48} DSC however did not reveal any melting, nor crystallization transitions. Poly-**1c** demonstrated good thermal stability through thermogravimetric analysis with a decomposition temperature (T_d) recorded at 5% mass loss, $T_d = 281$ °C. These thermal properties are promising for high-temperature applications and could be further manipulated through functionalization of the olefinic backbone.

Conclusions

In summary, this study demonstrates the potential of heterocyclic arynes as building blocks toward unique monomers and macromolecules. A key [4 + 2] cycloaddition between 2,3-pyridynes and cyclopentadiene delivered a streamlined access to pyridinonorbornenes, a unique class of ROMP monomers. Fine tuning of the pyridinonorborene structure led to a ROMP process of **1c** with living characteristics despite the postulated coordination of the pyridine nitrogen to the Ru center. This addition to the ROMP toolbox opens the door to the precise synthesis of pyridine-containing polymers as alternatives to PVPs with higher T_g . Potential applications range from metal capture to polymer self-assembly. Finally, this work demonstrates that modulation of the steric hinderance is a viable and protecting-group-free strategy for controlled ROMP of Lewis-basic monomers.

Author contributions

S. N. H., N. Y., and S. M. V. performed research. All authors designed research and analyzed data. Q. M., S. N. H., and N. Y. wrote the paper and supplementary materials. S. N. H. and N. Y. contributed equally to this study.

Conflicts of interest

There are no conflicts to declare.

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