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Tandem ROMP−Hydrogenation with a Third-Generation Grubbs Catalyst

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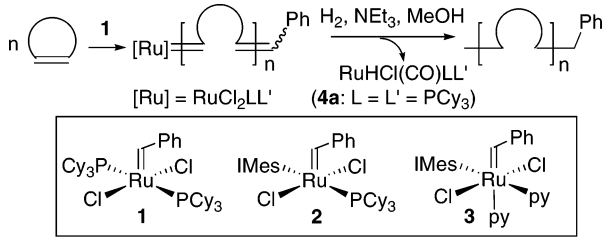
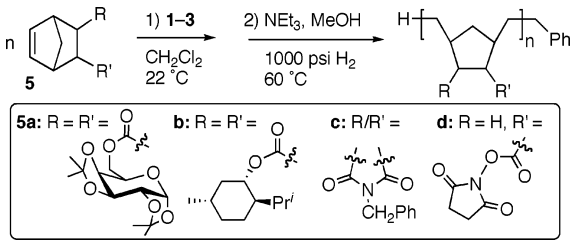
Tandem catalysis has attracted much interest for the power, economy, and process efficiencies that result from coupling multiple catalytic transformations in a single vessel.[1] Among such processes, tandem ROMP−hydrogenation (ROMP = ring-opening metathesis polymerization) enjoys a high profile as an efficient "back-door" route to functionalized polyolefins inaccessible by other means.[2] ROMP−hydrogenation of sterically unencumbered cyclooctenes using the Grubbs catalyst **1** is particularly well established. Reduction is optimally achieved by liberating the ruthenium end group on the polymer as hydrogenation-active **4a**, through reaction with H_2, base, and methanol (Scheme 1).[2d,3] These methodologies are equally applicable to other, less demanding metathesis−hydrogenation reactions mediated by **1**. Surprisingly, however, ROMP−hydrogenation is unexplored with second- or third-generation Grubbs catalysts (e.g., **2**,[4] **3**), despite their much higher reactivity, which could bring more challenging targets within reach. Here we describe precise, controlled, and efficient methodologies based on these catalysts and their application to the synthesis of functionalized polynorbornanes.

Scheme 1. Tandem ROMP−Hydrogenation and Catalysts Explored (IMes = *N*,*N*′-bis(mesityl)imidazol-2-ylidene, py = pyridine)



Functionalized norbornenes (NBEs) have been extensively used to construct "designer" ROMP materials.[5] Unlike cyclooctenes, with which backbiting and chain-transfer reactions are facile, NBEs undergo living ROMP with appropriate initiators, enabling precise specification of polymer chain lengths and block architecture. NBE-based ROMP materials include supported catalysts and reagents for organic synthesis,[6] recognition arrays relevant to cell signaling[7] and DNA diagnostics,[8] drug delivery[9] and antibacterial[10] materials, and photo- and electrochromic devices and transistors.[11,12] In many of these applications, the vulnerability of the unsaturated polymers to thermal, chemical, and photochemical degradation is a concern.[2,6a] While ROMP−hydrogenation offers a potentially attractive solution, particularly given the ineffectiveness of conventional hydrogenation methods,[13] limitations emerge from the decreased solubility characteristic of the saturated polymers. While this can be alleviated by use of disubstituted monomers, our **1**-based methodology is limited by the inefficiency of **1** in ROMP of these sterically encumbered substrates. Nomura and co-workers have noted that even monosubstituted NBEs can be slow to polymerize, if pendant groups are large;[14] the bulk of protecting groups is also important.[15]

Scheme 2. Tandem ROMP−Hydrogenation of Monomers **5a**−**d**



Progressively more demanding are *endo*,*exo*- or *endo*,*endo*-disubstituted 5,6-norbornenes. Hydrogenation poses its own problems, as indicated by findings from the Nguyen group that long-chain poly(NBE)s that are readily prepared by ROMP are reduced only with considerable difficulty.[16] As examples spanning these challenges, we chose monomers that probe different problems in ROMP: disubstituted *endo*,*exo*-NBEs bearing galactose (**5a**)[17] or menthol (**5b**) groups; *endo*,*endo*-dicarboximide NBE (**5c**), and a long-chain succinimide polymer, $[\mathbf{5d}]_{800}$, expected to resist hydrogenation (Scheme 2). Kiessling's pioneering work on related ROMP materials[7] points toward the potential of the saturated neoglycopolymers in biological applications (our own interest stemming from their potential in tissue engineering) and of the succinimide polymers as precursors to functionalized ROMP polyolefins.[7b,18] ROMP of **5a**−**c** by **1** was predictably inefficient, as illustrated for **5a**/**c** in Figure 1a. Where ROMP via second-generation initiators is fast but uncontrolled,[5,19] third-generation catalyst **3** enables both high reactivity and precise specification of chain lengths, with polydispersities as low as 1.02 (Figure 1a and Table 1). The Grubbs,[20] Slugovc,[21] and Kiessling[7b] groups recently reported the excellent performance of related pyridine/H_2IMes catalysts: **3** joins this category of outstanding Ru ROMP initiators.

While considerably superior to **1** and **2** for ROMP, **3** performed less well in tandem hydrogenation, as exemplified for $[\mathbf{5a}]_{50}$ in Figure 1b. In these experiments, we used the protocol we had optimized for **1**, adding CH_2Cl_2, NEt_3, and methanol in the glovebox once ROMP was complete, transferring the solution to an autoclave, and heating to 60 °C under 1000 psi H_2.[2d] Essentially identical activity is found for **1** and **2** (Figure 1b), with complete reduction of the ROMP polymer within 3 h. (This is not unexpected: the isolated hydride complexes $RuHCl(CO)(PCy_3)(L)$ (**4a**: L = PCy_3;

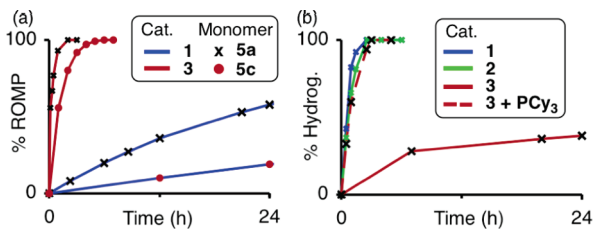


Figure 1. Selected representative reaction profiles: (a) ROMP via **1** or **3**; (b) tandem hydrogenation of $[\mathbf{5a}]_{50}$. For details, see Table 1 and Scheme 3.

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Table 1. Catalyst Performance and Polymer Properties[a]

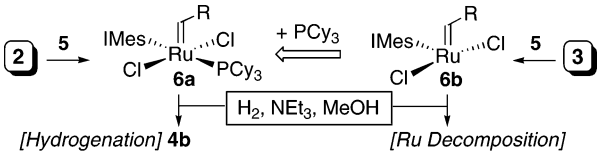
		ROMP		hydrogenation	
monomer	catalyst	time	$M_n \times 10^{-3}$ (PDI)[b]	% conv (time)	$M_n \times 10^{-3}$ (PDI)[b]
5a	**1**	3 days	40.2 (1.02)	100 (2.5 h)	40.7 (1.02)
5a	**2**	3 h	103.4 (1.3)	100 (2.6 h)	104.2 (1.3)
5a	**3**	2.5 h	32.8 (1.02)	38 (24 h)	
				+PCy_3: 100 (3 h)	33.2 (1.02)
5b	**3**	3 h	21.7 (1.03)	42 (24 h)	
				+PCy_3: 100 (4 h)	22.3 (1.02)
5c	**1**	7 days			
5c	**3**	6 h	14.9 (1.12)	100 (1 h)	15.0 (1.10)
5d[c]	**3**	0.5 h	12.3 (1.02)	96 (1.5 h)	
				+PCy_3: 100 (1.5 h)	13.7 (1.04)
5d[c,d]	**3**	8 h	189 (1.24)	70 (24 h)	
				+PCy_3: 100 (5 h)	*d*

[a] Typical ROMP conditions: [**5**]/[Ru] = 50, CH_2Cl_2, 22 °C; time to 100% except **1**/**5c** (70%). Hydrogenation: added CH_2Cl_2, NEt_3, MeOH; +1.2 equiv of PCy_3 if specified; 1000 psi H_2, 60 °C. [b] Calcd M_n (kDa): $[\mathbf{5a}]_{50}$, 33.3; $[\mathbf{5b}]_{50}$, 22.9; $[\mathbf{5c}]_{50}$, 12.7; $[\mathbf{5d}]_{50}$, 11.8, $[\mathbf{5d}]_{800}$, 188.1. [c] ROMP at −20 °C. [d] 800 equiv **5d**; saturated $[\mathbf{5d}]_{800}$ incompletely soluble in CH_2Cl_2.

4b: L = IMes) exhibit near-identical activity under similar conditions.)[22] In contrast, hydrogenation via **3** reaches only 40% after 48 h. Indeed, **3** proved effective in hydrogenating only $[\mathbf{5c}]_{50}$: for $[\mathbf{5b}]_{50}$, hydrogenation leveled off at ca. 40% after 24 h; for $[\mathbf{5d}]_{800}$, at 70%, consistent with catalyst decomposition before hydrogenation is complete.

We attribute the higher hydrogenation activity of **1** and **2** to the coordinating ability of PCy_3, which stabilizes the resting state of the catalyst (cf. **6a**, Scheme 3), inhibiting decomposition. Mol and co-workers have described formation of hydridocarbonyl complexes of type **4** as the major products on reaction of **1** and its N-heterocyclic carbene (NHC) derivatives with methanol.[23] We find that exposure to methanol decomposes **3** and its propagating species **6b** into ill-defined, catalytically incompetent Ru species within minutes. Neither pyridine nor a chelated carbonyl group on the subtended polymer chain in **6b**[24] provides a donor ligand strong enough to form a stable hydride complex analogous to **4**. The efficacy of PCy_3 as a stabilizing agent led us to hope, however, that we might gain access to the hydrogenation activity of **2**/**6a**, without sacrificing the remarkable ROMP efficiency of **3**, by deliberately trapping propagating species **6b** by post-ROMP addition of PCy_3. Indeed, addition of PCy_3 (1.2 equiv) following ROMP via **3**, prior to hydrogenolysis, proved strikingly effective. Hydrogenation of $[\mathbf{5a}]_{50}$ was restored to the levels achieved with **2** (Figure 1b). Similar efficiency is found for $[\mathbf{5b}]_{50}$ and $[\mathbf{5d}]_{800}$, with minimal perturbation of chain lengths (Table 1).

Scheme 3. Resting States in ROMP via **2** and **3** and Their Behavior under Conditions of Hydrogenolysis (R = poly[**5**] chain)



This "assisted tandem catalysis" process,[1b] in which we manipulate both the active site and the ancillary ligands to transform a highly active ROMP catalyst into a highly active, ligand-stabilized hydrogenation catalyst, enables us to convert sterically demanding monomers and a long-chain polymer into saturated, chain-length-precise polymers on a time scale of hours.

Of the metathesis catalysts now known, none offers the essential combination of features—high ROMP activity, controlled polymerization, and high hydrogenation activity—to transform challenging norbornene monomers into saturated polymers with precisely specified chain lengths. Here we integrate the outstanding ROMP performance of third-generation catalyst **3** with the high, sustained hydrogenation activity of **2**, by utilizing **3** as the ROMP initiator, then inducing post-ROMP transformation of the Ru end group into that formed via **2**. This approach offers a powerful, efficient solution to the problem of reconciling high reaction rates in demanding ROMP *and* hydrogenation reactions, while retaining precise control over polymer chain lengths. It is thus likely to find widespread application in the burgeoning area of ROMP-based "designer materials".

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Supporting Information Available: Experimental details, including rate curves for tandem hydrogenation reactions. This material is available free of charge via the Internet at http://pubs.acs.org.

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