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Communication

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Enol Ethers Are Effective Monomers for Ring-Opening Metathesis Polymerization: Synthesis of Degradable and Depolymerizable Poly(2,3-dihydrofuran)

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Supporting Information Placeholder

ABSTRACT: Enol ethers are widely used as quenching reagents for Grubbs catalysts. However, we report the surprisingly effective ring-opening metathesis polymerization (ROMP) of cyclic enol ethers, because the resulting electron-rich ruthenium alkylidene complex remains active towards metathesis of electron-rich olefins, despite its deactivation toward hydrocarbon olefins. We demonstrate the first example of ROMP of cyclic enol ethers, using 2,3-dihydrofuran as the monomer, producing a new type of degradable and depolymerizable poly(enol ether). The polymers exhibited perfect regioregularity and their molecular weights can be regulated using the loading of Grubbs initiators or the use of a linear vinyl ether as the chain transfer agent. We also developed protocols to deactivate the catalyst following metathesis of enol ethers and cleave the catalyst off the resulting polymers using H_2O_2 oxidation. The resulting poly(dihydrofuran) can be recycled to monomer via depolymerization with Grubbs catalyst or degraded to small molecules by hydrolysis under acidic conditions. This work opens exciting opportunities for a new class of ROMP monomers that lead to degradable polymers.

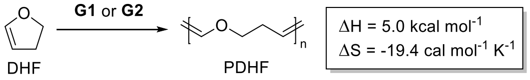
Ring-opening metathesis polymerization (ROMP) has emerged as a powerful method to synthesize a wide variety of polymers from cyclic olefinic monomers.[1] In a typical ROMP procedure using Grubbs catalysts, excess vinyl ether (a terminal enol ether) is added at the end of the polymerization to quench the catalyst by forming an electron-rich Ru carbene.[2-9] This so-called Fischer carbene is more thermodynamically stable than the propagating Grubbs alkylidene and has significantly reduced activity towards further metathesis reaction with olefins.[10] Therefore, vinyl ethers have been widely conceived as terminating agents for ROMP, and ROMP of cyclic enol ethers would seem impossible and has never been investigated. However, the Ru Fischer carbene has been shown to be not completely deactivated and may still act as a competent, albeit slow, metathesis catalyst for ROMP or ring-opening cross metathesis of cyclic olefins, particularly under elevated temperature or photochemical conditions.[10-14] Grubbs and coworkers further showed that Ru Fischer carbenes formed from terminal vinyl ethers, vinyl sulfides, and enamines can undergo further metathesis with these electron rich olefins.[10, 15] Intrigued by these observations, we became curious if *in situ* formed Ru Fischer carbene can indeed catalyze ROMP of cyclic enol ethers, despite the common belief that they are quenching reagents for Grubbs catalysts. If successful, this would enable a new family of monomers for ROMP, leading to a novel class of degradable polymers, poly(enol ether)

To test our hypothesis, we selected 2,3-dihydrofuran (DHF), an inexpensive, commercial cyclic enol ether as a potential monomer, considering that cyclopentene has similarly low strain but undergoes equilibrium ROMP.[16-20] To probe the ROMP reactivity of DHF, neat monomer was subjected to first and second generations of Grubbs catalysts, **G1** and **G2**, at room temperature. Both of these catalysts polymerized DHF to produce a rubbery polymer with T_g = -50.5 °C and thermal stability up to 320 °C (Figures S1 and S2). At $[DHF]_0/[Ru]_0 = 4000$, ROMP of DHF using **G1** under nitrogen with degassed monomer became too viscous to stir after 24 h at 55% conversion, yielding PDHF with M_n = 80 kDa, and M_n decreased to 56 kDa with $Đ$ = 1.3 after 3 days (Figure S3a). With more robust **G2**, ROMP of DHF was simply performed under air using non-degassed commercial DHF. The ROMP solution solidified in 15 min at 15% monomer conversion, yielding a polymer with M_n = 309 kDa and $Đ$ = 1.4, and the ROMP reached equilibrium after 4 h to form PDHF with M_n = 47 kDa and $Đ$ = 1.6 and 80% DHF conversion (Figure S3b).

To quantify conversions and better understand the polymerization thermodynamics of DHF, we needed a method to stop the ROMP of enol ether and prevent re-equilibration when the neat samples were diluted for NMR spectroscopy. Tricyclohexyl phosphine (PCy_3) is a strongly coordinating ligand,[21] and we found that the dissolution of the polymerization mixture into a solution containing 40 mM PCy_3 was sufficient to inhibit metathesis activity (Figure S7). Using this protocol, we measured the conversion using NMR analysis of the crude polymerization after ROMP reached equilibrium at 6, 22, and 40 °C with 0.05 mol% **G2**. At 22 °C, the reaction reached 76% conversion, corresponding to a residual monomer concentration of 3.2 M. Similarly, we determined the equilibrium DHF conversion at 6 and 40 °C to be 83% and 56%, respectively, corresponding to equilibrium monomer concentrations of 2.2 and 5.9 M. Using these values, we calculated the thermodynamic parameters for ROMP of neat DHF to be ΔH (neat) = -5.0 kcal mol^{-1} and ΔS (neat) = -19.4 cal mol^{-1} K^{-1} (Figure S9-S10, Table S1). These values are similar to those reported by Grubbs for ROMP of cyclopentene (in toluene-*d*8): ΔH = -5.6 kcal mol^{-1} and ΔS = -18.5 cal mol^{-1} K^{-1}.[17]

^1H NMR spectroscopy of isolated PDHF revealed that the polymerization proceeded with complete head-to-tail regioselectivity regardless of the catalyst used (Figure 1), which is consistent with the high regioselectivity of vinyl ether addition to Grubbs catalysts.[4, 8, 10] Throughout the polymerizations, an *E*:Z ratio around 4:6 to 1:1 was determined for the backbone olefins based on the integrations of olefin signals.

Table 1. Romp of 2,3-Dihydrofuran.[a]



Entry	$[DHF]_0$: $[I]_0$: $[CTA]_0$ [b]	Cat.	Temp. (°C)	$M_{n,MALLS}$ (kDa)[c]	Đ[d]
1	2000 : 1 : 0	**G1**	22	34.9	2.66
2	4000 : 1 : 0	**G1**	22	56.3	1.35
3	500 : 1 : 0	**G2**	22	6.0	2.14
4	1000 : 1 : 0	**G2**	22	9.9	1.43
5	2000 : 1 : 0	**G2**	22	30.1	1.70
6	4000 : 1 : 0	**G2**	22	47.4	1.60
7	8000 : 1 : 0	**G2**	22	92.9	1.77
8	10200 : 1 : 0	**G2**	22	127.7	1.35
9	2000 : 1 : 0	**G2**	6	36.0	2.05
10	2000 : 1 : 0	**G2**	40	24.5	1.99
11	1000 : 1 : 5	**G2**	22	5.69	1.80
12	1000 : 1 : 10	**G2**	22	2.83	2.10
13	1000 : 1 : 20	**G2**	22	1.63	1.89
14	1000 : 1 : 50	**G2**	22	0.65	2.31
15	1000 : 1 : 100	**G2**	22	0.29	2.61

[a] ROMP was performed using neat DHF under ambient atmosphere for 4 h (using **G2**) or N_2 atmosphere for 72 h (using **G1**), and quenched with basified H_2O_2. [b] Initial equivalents of DHF:Grubbs initiator:ethyl vinyl ether. [c] Determined by GPC MALLS analysis in THF. [d] M_w/M_n.

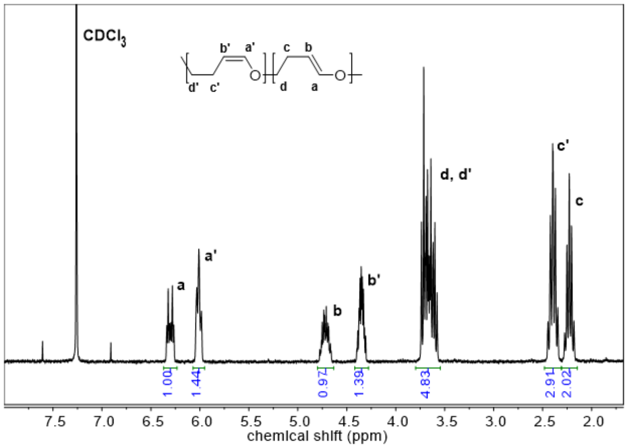


Figure 1. ^1H NMR spectrum of PDHF synthesized using **G2** at 22 °C.

We regulated the MWs of PDHF by varying the catalyst loading (Table 1, entry 1-8). M_n scaled linearly with $[DHF]_0/[\mathbf{G2}]_0$, ranging from 6 to 125 kDa as $[DHF]_0/[\mathbf{G2}]_0$ was varied from 500 to 10000 (Figure S4). Notably, even at 0.01 mol% catalyst loading, PDHF of MW >100 kDa could be obtained. In ROMP of low-strain hydrocarbon cyclic olefins, a linear internal olefin is often used as a chain transfer agent (CTA) to regulate MW.[22-25] We hypothesized that a linear enol ether, such as simple ethyl vinyl ether, could be used as a CTA in ROMP of cyclic enol ethers. Indeed, the MWs of the resulting polymers were directly proportional to the $[DHF]_0/[CTA]_0$ ratio, ranging from 5700 to 290 Da as $[DHF]_0/[CTA]_0$ was varied from 5 to 100 (Table 1, entry 11-15 and Figure S5).

Despite the extensive studies of cross metathesis between different hydrocarbon olefins, we are not aware of any previous study on cross metathesis between enol ethers. In order to better probe the secondary metathesis evident in the polymerization of DHF, we monitored the cross-metathesis between 1-(hexyloxy)hex-1-ene (2:1 mixture of *Z* and *E* isomers, totaling 90 mM) and ethyl vinyl ether (180 mM) catalyzed by **G2** (2.5 mM) at room temperature using GC (Figure S13). The observed equilibration time is similar to that of cross metathesis of common hydrocarbon olefins with **G1** but is roughly an order of magnitude slower than that with **G2**.[26-27] This finding provides useful guidelines to design ROMP of other cyclic enol ethers in the future.

Since ethyl vinyl ether is an effective CTA, we cannot use excess vinyl ether to remove the chain end Ru via exchange reactions. It was thus necessary to develop a new strategy to quench and remove Ru for ROMP of cyclic enol ethers. Hydrogen peroxide has been shown to rapidly oxidize Grubbs catalyst to ruthenium(IV) oxide and allow removal of Ru via filtration through silica,[28] so we hypothesized that this oxidation may be used to terminate the polymerization and cleave Ru off the polymer chain end. Since H_2O_2 solution is slightly acidic, to prevent any acid-catalyzed hydrolysis of poly(enol ether), an alkaline solution of 30% H_2O_2 in water was added dropwise to rapidly stirring polymer solution in THF with added PCy_3 (> 10 equiv. relative to catalyst). During this addition, the polymer precipitated as a white solid or a clear, colorless viscous material depending on the polymer MW. Low MW (M_n < 5 kDa) polymers that do not precipitate were purified by extraction into chloroform, filtration through silica, and concentration *in vacuo*.

In order to identify the chain-end functionality of PDHF terminated by H_2O_2 oxidation, tetraethylene glycol monomethyl vinyl ether was selected as a model compound. Grubbs catalyst was reacted with tetraethylene glycol methyl vinyl ether in THF, and the catalyst was subsequently reacted with alkaline 30% H_2O_2 (See SI for details). We identified the isolated product as tetraethylene glycol monomethyl ether formate by ^1H and ^{13}C NMR spectroscopy and mass spectrometry (Figure S20-21). ^1H NMR spectroscopy of an isolated PDHF quenched with H_2O_2 also showed the characteristic formate signal at 8.1 ppm. Further, the intensity of this formate end group signal matched that of the phenyl chain end from the benzylidene of the Grubbs initiator at equal stoichiometry, suggesting complete oxidative termination of all active chain ends (Figure S12).

The ability of PDHF to depolymerize and degrade is attractive for a circular economy. We examined the metathesis depolymerization of PDHF by adjusting conditions to shift the ROMP equilibrium toward monomer formation. A PDHF sample was prepared with 0.01 mol% **G2** and allowed to equilibrate for 3 h at room temperature. Without removal of the catalyst, the resulting solid polymer was warmed to 60 °C under flowing N_2 gas to remove monomer. After only 2.5 h, > 90% of pure monomer was recovered by condensation (Figure 2). This demonstration shows the facile and clean depolymerization of PDHF under mild conditions.

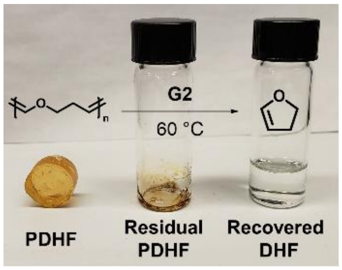


Figure 2. Facile depolymerization of PDHF to DHF.

Degradable ROMP polymers are desired but rare.[29-31] The abundant backbone enol ether linkage in PDHF makes it degradable under acidic conditions. PDHF after H_2O_2 quenching was dissolved in THF in the presence of 135 mM water and 25 mM acid and degraded at different rates depending on the strength of the acid. Acid-dependent degradation rate is expected because olefin protonation is the rate limiting step of enol ether hydrolysis.[32] When HCl was used, complete degradation to small molecules occurred in < 10 min as observed by GPC (Figure 3). When trifluoroacetic acid (TFA) was used, the MW of PDHF decreased over several hours (Figures 4, S14). Because the polymer hydrolysis follows 1st order reaction kinetics in both proton concentration and enol ether concentration, the inverse of M_n is expected to increase linearly with time.[33-35] Indeed, this trend was observed (Figure 4), indicating that polymer hydrolysis can be tuned by acid identity, acid concentration, and water concentration.

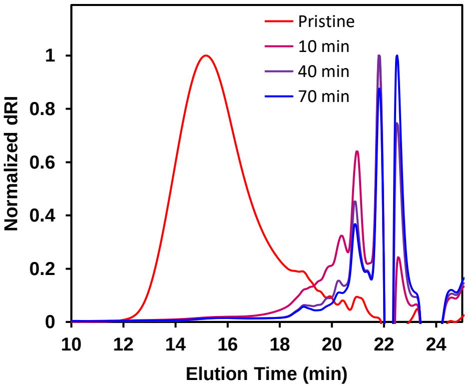


Figure 3. GPC analysis of PDHF hydrolysis in THF with 135 mM water and 25 mM HCl.

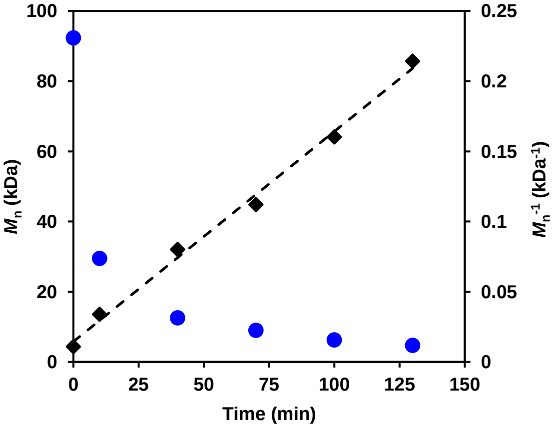


Figure 4. Molecular weight (blue circles) and inverse molecular weight (black diamonds) of PDHF during hydrolysis using TFA.

Following degradation of PDHF, no residual enol ether was observed by ^{1}H NMR spectroscopy. Degradation gave a mixture dominated by 4-hydroxybutanal and its cyclic hemiacetal isomer, 2-hydroxytetrahydrofuran, identical to that from the hydrolysis of DHF under the same conditions (Figure S16). Because hydrolyzed poly(enol ether)s revert to hydrolyzed monomer, the identity of degradation products can be controlled via design of monomer structures.

Interestingly, despite its rapid degradation in solution, solid PDHF has relative stability in an acidic environment. Following submersion of 54 kDa PDHF in aqueous HCl (0.1 M) for 24 h, M_n only decreased to 12 kDa (Figure S15). The slow solid-state degradation is favorable for extending the shelf life of PDHF during usage but allowing complete degradation eventually. We attribute the slow solid-state degradation to the hydrophobicity of PDHF: while the polymer backbone is highly susceptible to hydrolysis, slow penetration of water into solid samples becomes the rate limiting step in its degradation. Similar behavior has been recently reported for solid state degradation of polyacetals.[36]

In summary, we report the first example of effective ROMP of a cyclic enol ether under ambient conditions, despite the common belief that enol ethers are deactivating/quenching agents for Grubbs catalysts. We demonstrated that the *in situ* formed Ru Fischer carbenes are effective to catalyze ring-opening and cross metathesis of enol ethers and produce poly(enol ether)s in variable MWs. These results enable a new class of monomers for ROMP and generate a new type of depolymerizable and degradable polymers.

ASSOCIATED CONTENT

The Supporting Information is available free of charge on the ACS Publications website at DOI:

> Synthetic procedures and characterizations, ^{1}H and ^{13}C NMR spectra and GPC traces, determination of thermodynamic parameters, Fischer carbene quenching and inhibition study, cross metathesis study of internal enol ethers.

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Notes

The authors declare no competing financial interests.

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