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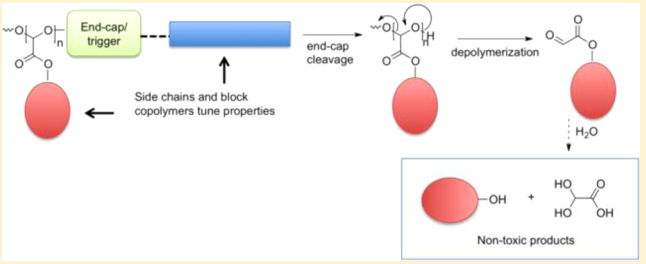
Polyglyoxylates: A Versatile Class of Triggerable Self-Immolative Polymers from Readily Accessible Monomers

Bo Fan,[†] John F. Trant,[†] Andrew D. Wong,[‡] and Elizabeth R. Gillies*[,†,‡]

[†]Department of Chemistry, and [‡]Department of Chemical and Biochemical Engineering, The University of Western Ontario, 1151 Richmond Street, London, Ontario N6A 5B7, Canada

Supporting Information

ABSTRACT: Self-immolative polymers, which degrade by an end-to-end depolymerization mechanism in response to the cleavage of a stabilizing end-cap from the polymer terminus, are of increasing interest for a wide variety of applications ranging from sensors to controlled release. However, the preparation of these materials often requires expensive, multistep monomer syntheses, and the degradation products such as quinone methides or phthalaldehydes are potentially toxic to humans and the environment. We demonstrate here that polyglyxoylates can serve as a new and versatile class of self-immolative polymers. Polymerization of the commercially available monomer ethyl glyoxylate, followed by end-capping with a 6-nitroveratryl carbonate, provides a poly(ethyl glyoxylate) that depolymerizes selectively upon irradiation with UV light, ultimately generating ethanol and the metabolic intermediate glyoxylic acid hydrate. To access polyglyoxylates with different properties, the polymerization and end-capping approach can also be extended to other glyoxylate monomers including methyl glyoxylate, *n*-butyl glyoxylate, and benzyl glyoxylate, which can be easily prepared from their corresponding fumaric or maleic acid derivatives. Random copolymers of these monomers with ethyl glyoxylate can also be prepared. Furthermore, using a multifunctional end-cap that is UV-responsive and also enables the conjugation of another polymer block via an azide−alkyne "click" cycloaddition, amphiphilic self-immolative block copolymers are also prepared. These block copolymers self-assemble into micelles in aqueous solution, and their poly(ethyl glyoxylate) blocks rapidly depolymerize upon UV irradiation. Overall, these strategies are expected to greatly expand the utility of self-immolative polymers by providing access for the first time to self-immolative polymers with tunable properties that can be readily obtained from simple monomers and can be designed to depolymerize into nontoxic products.



INTRODUCTION

In recent years, there has been significant interest in the development of degradable polymers for a wide range of applications including environmentally friendly plastics, adhesives, biomedical sutures, tissue engineering scaffolds, and drug delivery vehicles.[1−4] The preparation of biodegradable polymeric materials based on monomers derived from renewable, nonpetroleum resources is particularly attractive as these materials are potentially more sustainable than hydrocarbon-based materials and often degrade into nontoxic metabolic intermediates.[5,6] The development of stimuli-responsive polymers has also been a highly active area of research over the past couple of decades. Many examples of polymers undergoing changes in solubility or bond cleavage events in response to stimuli such as light,[7] changes in pH,[8] or redox potential,[9] and even mechanical force[10] have been reported with the aim of changing the properties of materials for applications such as tissue engineering, drug delivery, responsive coatings, and microfluidic valves.

Self-immolative linear polymers are materials that undergo end-to-end backbone depolymerization in response to the cleavage of stimuli-responsive end-caps.[11−13] They combine the features of both degradable and stimuli-responsive polymers, while having unique features such as a predictable dependence of degradation time on chain length[14] and the possibility to change the stimulus to which a given backbone responds, simply by changing the end-cap. Over the past several years, the field of self-immolative linear polymers has grown significantly and several different backbones have been developed including polycarbamates,[15−18] poly(carbamate-thiocarbamate)s,[19] polyphthalaldehydes,[20−23] and poly(benzyl ether)s.[24] Their application in a wide range of areas including sensors,[15,17] shape-changing plastics,[25] self-powered microscale pumps,[26] membranes,[27] and controlled release systems[16,28−30] has been explored. However, the multistep synthesis of monomers required for the preparation of these polymers, as well as their degradation into potentially toxic species such as quinone methides[31] and *o*-phthalaldehyde,[32] are potential barriers to the widespread application of these materials.

Polyglyoxylates are a potentially versatile new class of readily accessible self-immolative linear polymers. They are particularly

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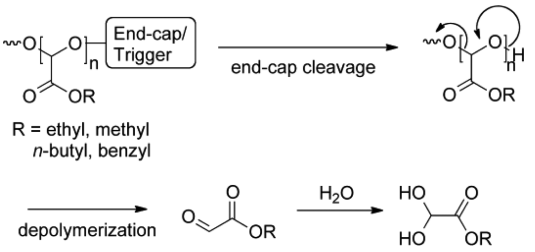
attractive, as monomers such as ethyl glyoxylate are directly available commercially on large scale. For example, ethyl glyoxylate (EtG) is prepared industrially via stepwise oxidation of acetaldehyde, which is a large-scale commodity chemical that can be obtained from petroleum feedstocks but also from bioethanol.[33] Poly(methyl glyoxylate) (PMeG) and poly(ethyl glyoxylate) (PEtG) have been previously reported, but rapidly depolymerize if not end-capped.[34−37] To address this, isocyanates, including phenyl isocyanate, have been introduced as end-capping agents.[37,38] Capped PEtG and PMeG have been shown to degrade by a combination of random backbone cleavage and depolymerization[39] to the corresponding alcohol as well as glyoxylic acid hydrate,[36,40] an intermediate in the glyoxylic acid cycle, and ultimately to CO_2 in the environment.[41] The degradation products of PEtG have been demonstrated to be nontoxic in invertebrate models and in plant ecotoxicity models.[41] To the best of our knowledge, this class of polymers has not yet been imparted with stimuli-responsive degradation properties, which should enable them to degrade selectively by the end-to-end depolymerization mechanism as shown in Scheme 1, making them a new class of self-immolative polymers.

Scheme 1. Depolymerization of Polyglyoxylates upon End-Cap Cleavage



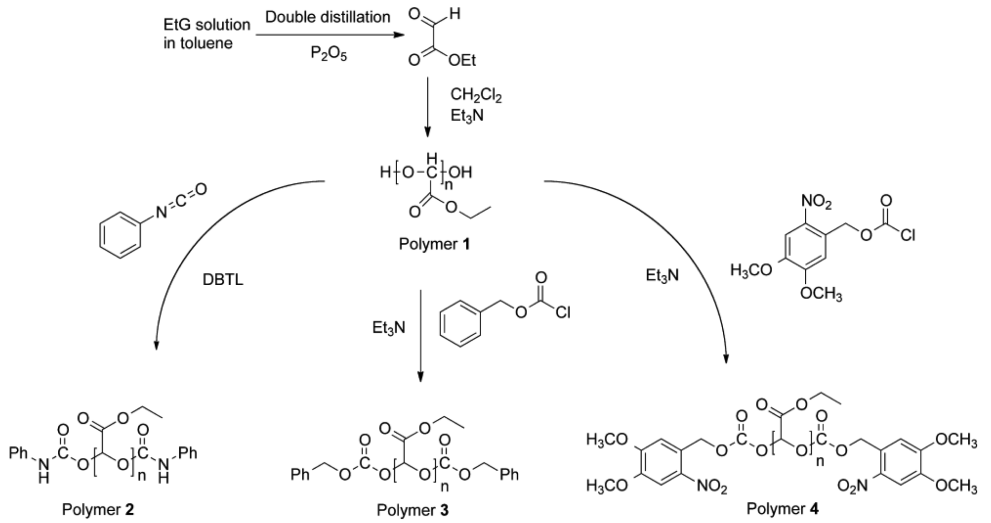
Using UV light as a model stimulus, we describe here the development of PEtG as a new self-immolative linear polymer. Furthermore, we demonstrate that various other glyoxylates including methyl glyoxylate (MeG), *n*-butyl glyoxylate (*n*-BuG), and benzyl glyoxylate (BnG) can be prepared in two steps from starting materials such as fumaric acid, which is a large-scale industrial chemical that can be prepared from petroleum sources[42] or from the agricultural byproduct furfural.[43] Both homopolymers and copolymers of these monomers with EtG can also be prepared. Moreover, amphiphilic block copolymers capable of self-assembly into micelles in aqueous solution can be prepared using a multifunctional end-cap. All of these polymers exhibit stimuli-responsive self-immolative degradation. The accessibility of the polymerization monomers both from petroleum and renewable resources as well as the depolymerization of PEtG in particular into nontoxic metabolic intermediates is anticipated to open numerous new prospects for self-immolative polymers.

RESULTS AND DISCUSSION

Synthesis and Characterization of PEtG with a Stimulus-Responsive End-Cap. Because of the availability of EtG from commercial sources on a large scale, this monomer was selected to demonstrate the feasibility of using polyglyoxylates as self-immolative materials. Purification of EtG is an essential prerequisite to obtain high molecular weight PEtG, as excess initiation and transfer reactions resulting from glyoxylate hydrate, water, or other impurities result in low molecular weight products. In our hands, the most effective purification protocol involved two successive distillations of the crude EtG at 130 °C over phosphorus pentoxide under argon at atmospheric pressure. The high temperature of the distillation ensured cracking of the glyoxylate oligomers, and the drying agent removed any liberated water. As shown in Scheme 2, the optimized conditions for polymerization involved the use of CH_2Cl_2 as a solvent at −20 °C in the presence of NEt_3. Under these conditions, residual trace water or ethyl glyoxylate hydrate (EtGH) initiates the polymerization providing PEtG **1**, which can be isolated by precipitation in methanol.

PEtG **1** can be end-capped in situ, by reaction with phenyl isocyanate in the presence of dibutyltin dilaurate (DBTL) to provide the control PEtG **2** as previously reported.[37,38] It was found that chloroformates also serve as efficient end-capping agents in the presence of additional NEt_3. For example, capping with benzyl chloroformate provided control PEtG **3** with a carbonate end-cap. To prepare a stimuli-responsive PEtG, 6-nitroveratryl chloroformate (NVOC-Cl) was selected as an end-cap to provide the nitroveratryl carbonate (NVOC) end-

Scheme 2. Synthesis of PEtG



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capped PEtG **4**. While the chloroformate chemistry can be used to potentially introduce a variety of end-caps, the NVOC group is ideal in the current work as a model end-cap because it is well-known that it can be cleanly cleaved with UV light (λ = 340 nm) under neutral conditions, which was expected to initiate the depolymerization of the polymer (Scheme 1).

All of the PEtGs were characterized by ^{1}H and ^{13}C NMR spectroscopy, IR spectroscopy, and size exclusion chromatography (SEC). The spectral data were consistent with the expected chemical structures (Supporting Information). As shown in Table 1, SEC results showed that PEtGs **1**−**4** have

Table 1. SEC Results for the Polymers, Measured in THF Relative to Polystyrene Standards and Thermal Properties Measured by TGA and DSC

polymer	M_n (kDa)	dispersity ($Đ$)	$T_{98\%}$ (°C)	T_g (°C)
1	103	2.6	84	−32
2	27	2.5	168	−1
3	31	1.9	161	−3
4	53	1.7	164	−9
11	3.8	1.3	139	25
12	5.0	1.9	180	−30
13	2.1	1.6	147	12
14	40	2.0	169	15
15	11	2.0	164	−10
19	42	2.1		
21	40	2.1	160	−5 (T_m = 46)

number-average molecular weights (M_n) ranging from 27−103 kDa with dispersities ($Đ$) of 1.7−2.6. The higher molar mass of the unend-capped polymer **1** may reflect the selective precipitation of the higher molar mass fraction of **1** as lower molar mass PEtG has been observed to precipitate slowly from methanol, which could allow depolymerization to occur during this process. However, it is also possible that the end-capping process, carried out at ambient temperature to increase the rate of end-capping, could potentially result in some degree of depolymerization and may favor chains with lower degrees of polymerization, which are more reactive. It was also noted that both the yield (e.g., 62% for **4**) and the molar mass were higher for the polymers end-capped with chloroformates in comparison with the less reactive isocyanate (e.g., 45% yield), suggesting that rapid end-capping may be important for preserving the degree of polymerization.

The thermal properties of the polymers were measured by thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC). TGA was particularly useful for differentiating between capped and uncapped polymers. On the basis of the maximum temperature at which 98% of mass is still present ($T_{98\%}$, Table 1), as well as all other measures of thermal stability (Supporting Information Table S2), the unend-capped PEtG **1** was less stable than the end-capped PEtGs **2**−**4**. The data suggest that **1** likely degrades thermally by depolymerization, whereas PEtGs **2**−**4** require a backbone or end-cap cleavage to initiate the thermal degradation process. All of the PEtGs were amorphous and exhibited glass transition temperatures (T_g) of −32 °C for the uncapped PEtG **1** and −9 to −1 °C for end-capped PEtGs **2**−**4** (Table 1).

Stimuli-Responsive Degradation of PEtG. The triggered degradation of PEtG **4** in response to irradiation with UV light was studied both in solution and in polymer films. PEtG was insoluble in fully aqueous conditions, but dissolved in 9:1 CD_3CN:D_2O at 15 mg/mL, a concentration sufficient for NMR studies. First, UV−visible spectroscopy was used to determine the required irradiation time for NVOC cleavage in this solution, and it was found that 80 min of irradiation with a low energy UV light source (300−350 nm) was sufficient to effect complete removal of the NVOC end-cap (Supporting Information Figure S46).

A comparison of the NMR spectra before and after irradiation supports the successful cleavage of the end-cap. Before irradiation, the spectrum consisted of three broad peaks attributable to the PEtG backbone, and peaks corresponding to the two methoxy groups (4.06 and 3.97 ppm) on the NVOC moiety were also observable. However, after irradiation and incubation in the solution at ambient temperature (21 °C) for 3 h, the peaks corresponding to the methoxy groups had disappeared, resulting in a series of small singlets between 3 and 4 ppm. This confirmed that the NVOC group had indeed been cleaved. In addition, as shown in Figure 1a, the broad peak at 5.6 ppm corresponding to the acetal hydrogens along the polymer backbone decreased in intensity, while a new sharp peak at 5.1 ppm corresponding to the expected degradation product EtGH emerged. Sharpening of the peaks corresponding to the ethyl group was also consistent with depolymerization to EtGH. On the basis of the relative peak integrations, about 50% of the PEtG had depolymerized into EtGH after 3 h, increasing to more than 70% after 24 h. In contrast, as shown in Figure 1b, a nonirradiated sample of PEtG **4** did not undergo any detectable degradation after 7 days in solution. In addition, PEtG **3** with the benzyl carbonate end-cap remained unchanged after UV irradiation and 7 days in solution (Supporting Information Figure S47). Combined, these data confirm that the depolymerization of PEtG **4** indeed results from backbone depolymerization induced by end-cap cleavage and not by random backbone cleavage induced by UV light or hydrolytic reactions.

PEtG's insolubility in water allows for the preparation and study of PEtG film degradation under aqueous conditions. Films were prepared and subjected to UV irradiation, then immersed in pH 7.4 phosphate buffer. At time points ranging from 1−17 days, the films were removed, rinsed, and dried, and then the remaining mass of polymer was measured. As shown in Figure 2a, the irradiated films of PEtG **4** exhibited steady mass loss over the 17 days, at which point they had completely degraded. In contrast, nonirradiated films of PEtG loss less than 4% of their mass during this same time period. This small amount of weight loss is likely due to a small degree of ester hydrolysis and backbone degradation, as PEtGs are known to gradually degrade in water.[40]

After the measurement of mass loss, the material remaining on the slide was analyzed by SEC to determine to what degree depolymerization had occurred, as small levels of nonspecific hydrolysis and/or slow depolymerization would result in a lower molecular weight, but may not result in dissolution of the material from the film. As shown in Figure 2b, the initial M_n of polymer **4** was 53 kDa, but after UV irradiation the M_n of polymer **4** decreased to about 37 kDa in the first day. Over the next 12 days, the M_n exhibited very little change, but at the same time the mass of the film kept decreasing. This suggests that the film was likely disintegrating via a surface erosion process during this time period so the M_n of the bulk material that remained unexposed to water was not affected. From days 13 to 17, a rapid reduction in molecular weight was observed, which, as shown in Figure 2a, correlated to the loss of the

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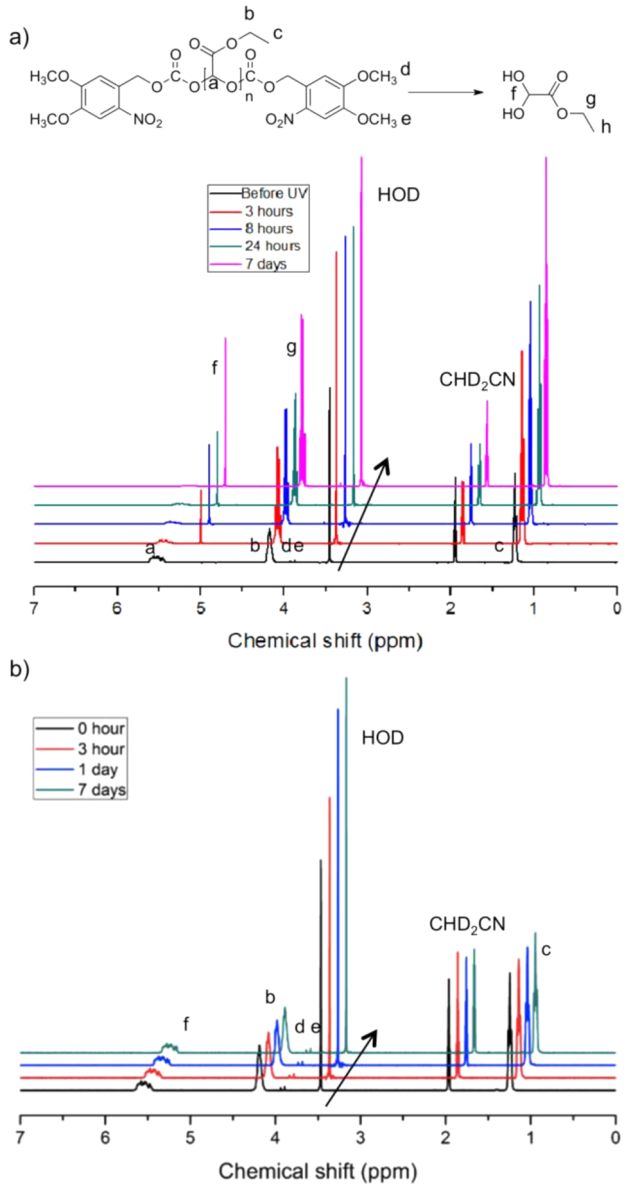

Figure 1. ^{1}H NMR spectra of PEtG **4**: (a) after UV irradiation and (b) without UV irradiation, following incubation in 9:1 CD_3CN:D_2O at 21 °C for varying time periods. Spectra are offset to allow the progression over time to be clearly observed. Additional spectral details are shown in Supporting Information Figures S48 and S49.

remaining 10% of material from the films. At this stage, with only a thin film of material remaining on the slides, the percentage of material exposed to water and thus depolymerizing progressively increased, resulting in a reduction of M_n for the measured sample. In comparison, the M_n of the nonirradiated control remained very close to that of the starting polymer throughout the experiment.

Development of Stimuli-Responsive Polyglyoxylates with Diverse Ester Side Chains. Having shown that PEtG can selectively undergo depolymerization in response to a stimulus, it was of interest to demonstrate that the simple structure of the monomer allows for the rapid generation of structurally diverse polymers using alternate glyoxylates. Glyoxylates other than EtG are available from specialty chemical suppliers, but at high cost. Therefore, we aimed to develop an improved synthetic route to access these monomers.

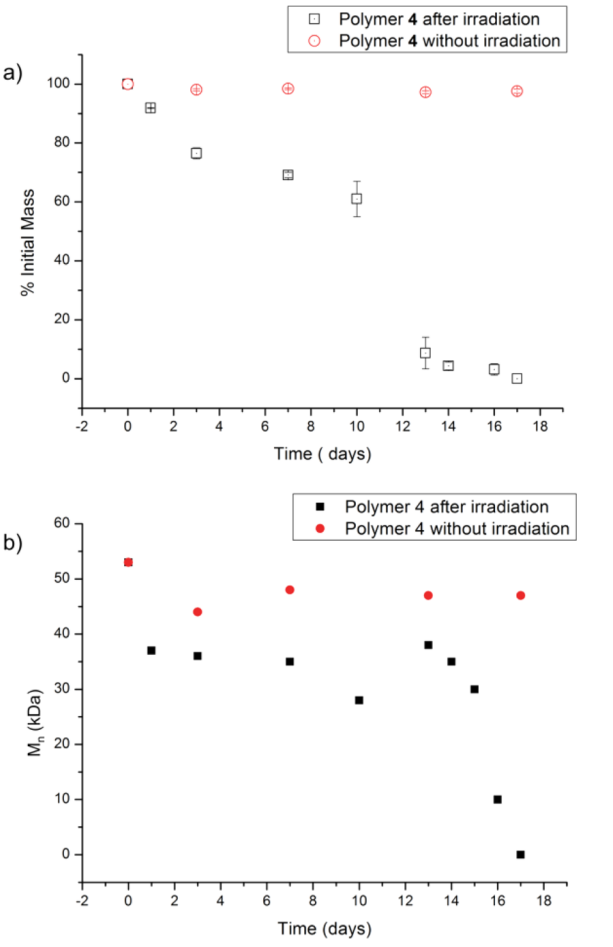

Figure 2. (a) Mass loss from films of PEtG **4** with and without UV irradiation upon incubation in pH 7.4 phosphate buffer. Error bars represent the standard error on the measurement of three films. (b) Evolution of molar mass in the same films as measured by SEC (one measurement per time point).

The most common synthetic approach toward glyoxylates is the oxidative cleavage of dialkyl tartrates.[44−46] However, this introduces oxidative impurities, such as the corresponding acid, that can be challenging to remove.[47,48] While the purity is sufficient for most synthetic applications, higher purity monomer is required for polymerization. To address this, ozonolysis of dialkyl fumarates and maleates was used as an alternative strategy.

As shown in Scheme 3, methyl maleate (**5**), *n*-butyl fumarate (**6**), and benzyl fumarate (**7**) were first prepared by standard esterification procedures. Ozonolysis with quenching by dimethyl sulfide, followed by distillation, provided the corresponding glyoxylates **8**−**10**. These monomers were polymerized using the same procedures as for PEtG **4** to provide poly(methyl glyoxylate) (PMeG, **11**), poly(*n*-butyl glyoxylate (PBuG, **12**), and poly(*n*-benzyl glyoxylate) (PBnG, **13**), each having a NVOC end-cap.

As shown in Table 1, the molecular weights of polyglyoxylates **11**−**13** were significantly lower than those of the PEtGs, with M_n ranging from 2.1−5.0 kDa and $Đ$ from 1.3−1.9. These values were in reasonable agreement with the M_n values obtained by ^{1}H NMR spectroscopy (Supporting Information Table S1). This may be related to lower reactivities of these monomers, but also may relate to the challenge of purifying these monomers to the same degree as for EtG. However, this

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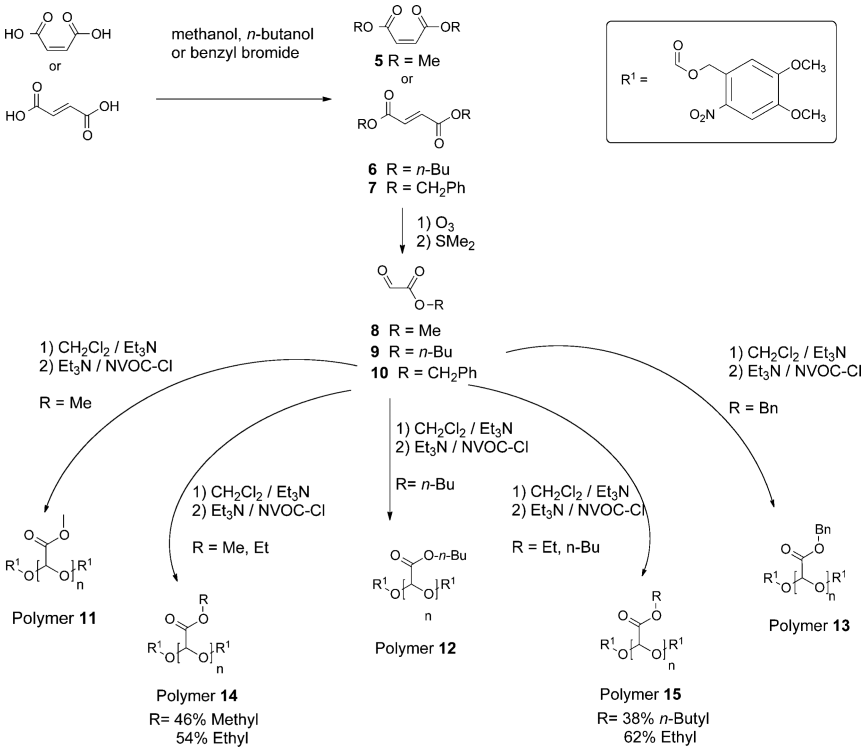
Scheme 3. Synthesis of Glyoxylate Monomers and Polyglyoxylates



limitation was overcome by preparing copolymers. Copolymerization of MeG **8** and EtG in a 55:45 feed ratio provided copolymer **14** comprising approximately 46:54 methyl:ethyl side chains and with an M_n of 40 kDa, comparable to that of the PEtG's despite the high MeG content. Similarly, *n*-BuG **9** was copolymerized with EtG in a 38:62 feed ratio to afford copolymer **15** comprising approximately 33:67 *n*-butyl:ethyl side chains.

As shown in Table 1, the thermal stabilities of these polyglyoxylates are similar to those of the end-capped PEtGs (**2**–**4**). DSC revealed that these polymers are amorphous with T_g's ranging from −30 to 25 °C. The T_g decreases as the length of the pendant alkyl group increases from methyl to butyl, which is expected as these flexible groups facilitate chain motion. On the other hand, polymer **13** with the less flexible benzyl side chain has an intermediate T_g of 12 °C. Copolymers **14** and **15** have T_g's that are between those of their corresponding homopolymers.

Polyglyoxylates **11**–**15** exhibited solubility properties similar to those of PEtG, and their stimuli-responsive degradation was therefore studied as described above for PEtG. In each case, irradiation with UV light in 9:1 CD_3CN:D_2O followed by incubation at 21 °C resulted in conversion of the broad peaks corresponding to the polymers in the ^{1}H NMR spectra to sharp peaks corresponding to the expected glyoxylate hydrates over a period of 7 days (Supporting Information Figures S50–S55). The degradation rates of the different polyglyoxylates are summarized in Figure 3, and individual graphs are provided in Supporting Information Figures S56–S62. In each case, the degradation approached completion in less than 10 days, with a small fraction of the resulting glyoxylate existing in its oligomerized form under these conditions. The differences in rates can likely be attributed to a combination of factors including differences in chain lengths,[14] the susceptibilities of the different polymers to depolymerization, and the reoligomerization of the liberated monomers under these conditions. In each case, nonirradiated samples were also studied and did not show any signs of degradation (Supporting Information Figures S50–S55). Overall, these results suggest that the different polyglyoxylates and their copolymers degrade similarly to PEtG, thereby opening prospects for the preparation of a wide variety of glyoxylate-based polymers.

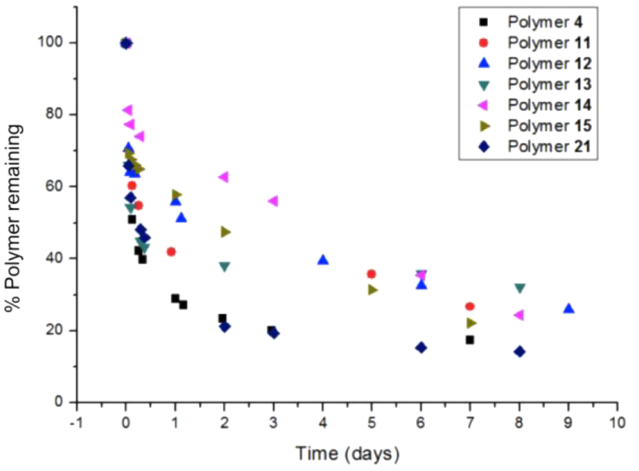


Figure 3. Depolymerization of different end-capped polyglyoxylates following cleavage of the NVOC end-caps by UV irradiation in 9:1 CD_3CN:D_2O followed by incubation at ambient temperature (21 °C). Individual data sets are available in Supporting Information Figures S56–S62.

Development and Study of Polyglyoxylate Block Copolymers. The preparation of block polymers is another strategy routinely used to modify the properties of polymeric materials. In the current work, we demonstrate this approach by the incorporation of a hydrophilic block onto the relatively hydrophobic PEtG block, thereby preparing an amphiphilic

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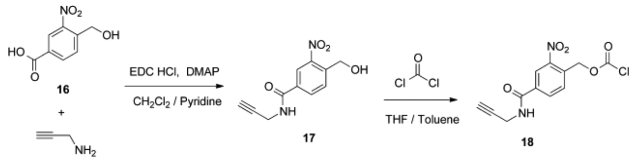
block copolymer. Poly(ethylene glycol) (PEG) was selected as the hydrophilic block as it is a water-soluble polymer that is still being extensively studied in a wide range of applications from coatings to drug delivery vehicles.[49,50] To incorporate the PEG block while at the same time retaining the ability of the PEtG to undergo stimuli-responsive depolymerization, it was necessary to develop a new multifunctional end-cap. As shown in Scheme 4, starting from the previously reported alcohol **16**,[51] the

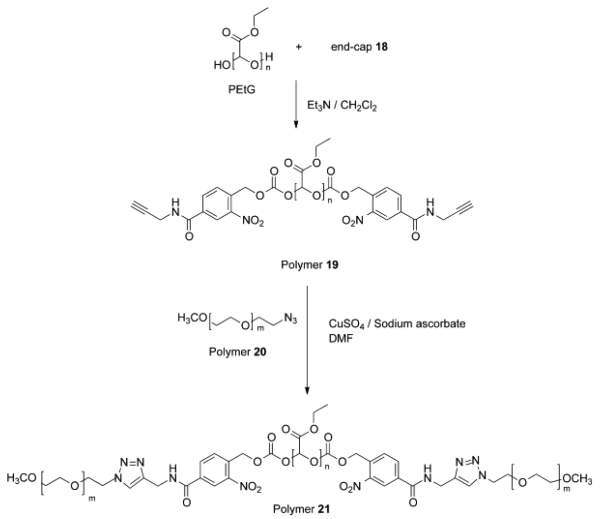
Scheme 4. Synthesis of a Multifunctional End-Cap



propargyl amide **17** was synthesized through an EDC-mediated coupling. Next, the alcohol group was converted into a chloroformate by reaction with phosgene to obtain the target linker end-cap **18**.

As shown in Scheme 5, PEtG was prepared and end-capped with chloroformate **18** to provide polymer **19**. A copper-

Scheme 5. Synthesis of a PEG−PEtG−PEG Triblock Copolymer



assisted azide−alkyne "click" cycloaddition (CuAAC) between **19** and azide-terminated PEG **20**[52] with a molar mass of 2 kDa provided PEG−PEtG−PEG triblock copolymer **21**. Excess PEG was removed by dialysis in water. As shown in Table 1 and Supporting Information Figure S34, SEC of **21** did not show any significant change in molar mass relative to polymer **19**, but it confirmed the absence of uncoupled PEG, and the presence of the expected amount of PEG in the ^{1}H NMR spectrum of **21** confirmed the successful coupling. As shown in Supporting Information Figure S35 and Table S2, TGA showed a two-phase degradation process for the material, with the initial mass loss corresponding to the PEtG block and the second phase corresponding to PEG. The relative mass losses for these two phases were consistent with the expected content of PEtG and PEG in **21**. Incorporation of the PEG also imparted semicrystalline properties to the material, with a T_g of −5 °C and a T_m of 46 °C. As shown in Figure 3, triblock copolymer **21** also underwent depolymerization triggered by UV light at a rate very similar to that of PEtG in CD_3CN:D_2O (9:1).

The self-assembly of amphiphilic triblock copolymer **21** in water was also studied. It was found that nanoprecipitation of a DMSO solution of **21** into water, followed by the removal of DMSO by dialysis, resulted in the formation of micellar nanoparticles with a *Z*-average diameter of 50 nm and a low polydispersity index of 0.06 as measured by dynamic light scattering (DLS) (Figure 4a). These micelles were also imaged by transmission electron microscopy (TEM) (Figure 4b).

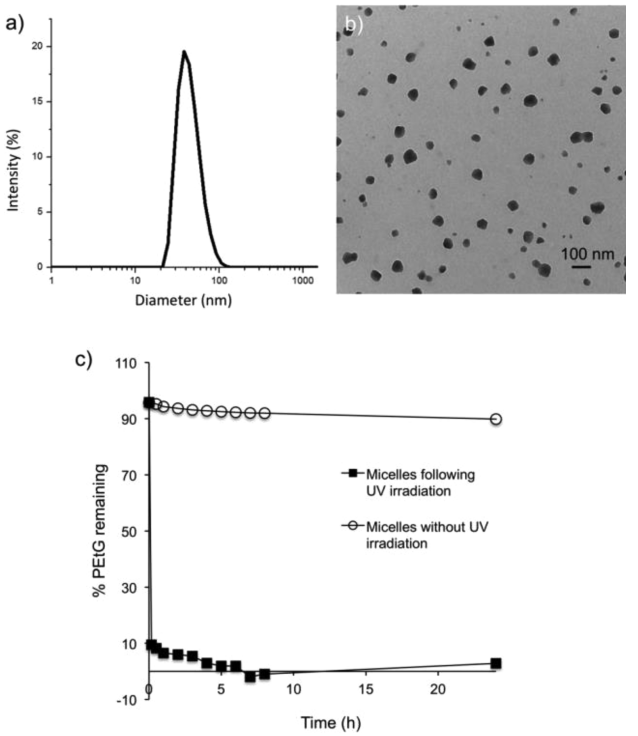


Figure 4. (a) Intensity distribution of micelle hydrodynamic diameters measured by DLS in water; (b) TEM image of micelles prepared in water; and (c) depolymerization of PEtG in micelles following UV irradiation in 5:1 100 mM, pH 7.4 phosphate buffered D_2O:DMSO-d_6 at 37 °C and comparison with a control nonirradiated sample of the micelles.

The self-assembly and depolymerization were also studied by ^{1}H NMR spectroscopy. In this case, the assemblies were prepared by nanoprecipitation of a DMSO-d_6 solution of the polymer into pH 7.4 phosphate buffered D_2O. For practical reasons, the DMSO-d_6 was not removed by dialysis. Consistent with the self-assembly of **21** into micelles under these conditions, only the peak corresponding to the PEG block and no peaks corresponding to the PEtG block were observed in the NMR spectrum prior to UV irradiation. However, a ^{1}H NMR spectrum taken immediately following UV irradiation showed greater than 90% degradation of PEtG block, as measured by the appearance of peaks corresponding to EtGH (Supporting Information Figure S63). Subsequently, the resulting EtGH underwent ∼45% hydrolysis to glyoxylic acid hydrate and ethanol over 24 h at 37 °C. These results show that the depolymerization following end-cap cleavage is much faster in these buffered aqueous conditions than in 9:1 CD_3CN:H_2O, and also that the nanoscale dispersion of PEtG into water through self-assembly of copolymer **21** results in much more

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rapid depolymerization than in films of pure PEtG. In contrast, a control sample of micelles that was not irradiated underwent less than 10% degradation over 24 h. Overall, this demonstrates that the preparation of block copolymers of PEtG is also an effective strategy for tuning the properties while at the same time retaining stimuli-responsive degradation.

CONCLUSIONS

It was demonstrated for the first time that, through the use of stimuli-responsive end-caps, polyglyoxylates serve as a new class of self-immolative linear polymer backbones. The use of chloroformates provides an effective end-capping strategy as demonstrated by the preparation and study of a control PEtG as well as a triggerable PEtG **4** with a UV light-cleavable end-cap. This will allow a variety of end-caps responsive to different stimuli to be incorporated into polyglyoxylates. It was also shown that glyoxylates with various side chains can be prepared by simple two-step synthetic processes starting from fumaric or maleic acid, and these can be homopolymerized or copolymerized with EtG to provide materials with a range of properties and molar masses. Furthermore, using a multifunctional end-cap, it is possible to prepare glyoxylate-based triblock copolymers, which provides an additional means of tuning polymer properties. All of the above materials underwent depolymerization to the expected products selectively upon cleavage of the end-cap, while the untriggered polymers were stable under the studied conditions. These new materials are particularly attractive as the component monomers can be derived not only from petroleum-based sources, but also from renewable resources. In addition, while the toxicity of other alcohol derivatives remains to be explored, PEtG depolymerizes to ultimately provide the benign products glyoxylic acid hydrate and ethanol. This should open many new prospects for the field of self-immolative polymers. Future work will involve further studies of the toxicity and properties of various polyglyoxyates available through this chemistry as well as the development of polyglyoxylate coatings and aqueous assemblies for controlled release, sensing, and other applications.

EXPERIMENTAL SECTION

Synthesis of PEtG 4 (Representative Polyglyoxylate Synthesis). EtG in toluene solution (20 mL) was fractionally distilled under vacuum (55 °C, 125 mbar) over P_2O_5 to remove toluene and trace water in the first, discarded fraction. The residue was then distilled twice successively over P_2O_5 at atmospheric pressure under argon at 130 °C to obtain the highly pure monomer. The resulting pale yellow liquid (5.0 mL, 50 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (5.0 mL) and Et_3N (3.5 μL, 25 μmol, 0.0005 equiv). The solution was stirred for 1 h at −20 °C. NVOC-Cl (0.2 g, 730 μmol, 0.014 equiv) and Et_3N (100 μL, 730 μmol, 0.014 equiv) were added at 0 °C to end-cap the polymer. The solution was then allowed to come to room temperature and stirred for 24 h at room temperature and a further 16 h at 40 °C. Purification was achieved by precipitation of the crude reaction mixture into methanol. After decanting the excess methanol, the residue was dried in vacuo for 48 h to provide 3.2 g of a white, sticky polymer in 62% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 0.04H), 7.01 (s, 0.02H), 5.48−5.75 (m, 312H), 4.06−4.34 (m, 642H), 4.05 (s, 6H), 3.97 (s, 6H), 1.17−1.45 (m, 963H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.8−166.4, 148.1, 107.9, 90.1−94.0, 86.9, 66.7, 61.9, 56.5, 55.1, 13.7. FT-IR (KBr, thin film): 2985, 1757, 1448, 1377, 1022 cm^{-1}. SEC: M_n = 53 kg/mol, M_w = 91 kg/mol, $Đ$ = 1.7, T_g = −9 °C.

Synthesis of *n*-BuG 9 (Representative Glyoxylate Synthesis). Diester **6** (26.0 g, 114 mmol, 1.0 equiv) was dissolved in CH_2Cl_2 (300 mL), and the solution was cooled to −78 °C in a dry ice/acetone bath. Ozone was bubbled into the solution under stirring until the solution turned into blue, and then the solution was purged with oxygen. Dimethyl sulfide (10.0 mL, 137 mmol, 1.2 equiv) was then added dropwise to quench the system. After being stirred for 5 h, and warmed to room temperature, the solvent and the residual dimethyl sulfide were removed by distillation at 70 °C under argon. A pale yellow liquid (15.3 g, 52%) was obtained after distillation at 150 °C (200 mbar) over P_2O_5. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.39 (s, 1H), 4.31 (t, J = 6.6 Hz, 2H), 1.68−1.76 (m, 2H), 1.37−1.47 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $(CD_3)_2SO$): δ 184.2, 159.7, 65.3, 30.0, 18.6, 13.4. MS calcd for $[M + H]^+$ $C_6H_{11}O_3$, 131.07082; found, 131.07088.

Synthesis of Propargyl Amide 17. Compound **16** (580 mg, 2.9 mmol, 1.0 equiv) was dissolved in solvent (12 mL of 5:1 CH_2Cl_2:pyridine), and then EDC·HCl (690 mg, 3.5 mmol, 1.2 equiv), propargyl amine (1.1 mL, 17.7 mmol, 6 equiv), and DMAP (430 mg, 3.5 mmol, 1.2 equiv) were added into the stirring mixture under argon. After being stirred at room temperature for 6 h, the reaction was diluted with ethyl acetate (60 mL) and washed with saturated $NaHCO_3$ solution (1 × 30 mL), 1 M HCl (3 × 30 mL), and deionized water (1 × 30 mL) successively. The organic phase was dried with $MgSO_4$, filtered, and the solvent removed under reduced pressure to yield compound **17** (395 mg, 57%) as a brown solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ 9.26 (t, J = 5.3 Hz, 1H), 8.53 (d, J = 1.2 Hz, 1H), 8.22 (dd, J = 7.6 Hz, 1.2 Hz, 1H), 7.94 (d, J = 7.6 Hz, 1H), 5.67 (t, J = 5.3 Hz, 1H), 4.87 (d, J = 5.3 Hz, 2H), 4.09 (dd, J = 5.3 Hz, 2.4 Hz, 2H), 3.16 (t, J = 2.4 Hz, 1H). ^{13}C NMR (150 MHz, $(CD_3)_2SO$): δ 163.7, 146.4, 141.6, 133.0, 132.0, 128.4, 123.1, 80.7, 73.0, 59.8, 28.6. MS calcd for $[M]^+$: $C_{11}H_{10}O_4N_2$, 234.0641; found, 234.0642.

Synthesis of Chloroformate 18. Caution: Phosgene is a highly toxic gas and must be handled with great care; refer to the MSDS before using. Compound **17** (390 mg, 1.6 mmol, 1.0 equiv) was dissolved in THF (7 mL). The resulting solution was then added dropwise into a phosgene solution (15 wt % in toluene, 3.5 mL, 4.8 mmol, 3.0 equiv) under an argon atmosphere at room temperature and was stirred for 40 h. The residual phosgene and solvent were then removed by high vacuum to yield compound **18** (482 mg 98%) as a brown solid. Phosgene collected in the liquid nitrogen-cooled trap was then quenched with methanol (10 mL) and saturated sodium hydroxide solution (10 mL). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.59 (d, J = 2.0 Hz, 1H), 8.17 (dd, J = 8.2 Hz, 2.0 Hz, 1H), 7.79 (d, J = 8.2 Hz, 1H), 6.36 (s, 1H), 5.81 (s, 2H), 4.31 (dd, J = 5.1 Hz, 2.3 Hz, 2H) 2.35 (t, J = 2.3 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 164.1, 150.6, 135.49, 133.4, 132.8, 132.3, 129.5, 124.1, 78.8, 72.8, 69.1, 30.4. MS calcd for $[M]^+$: $C_{12}H_9O_5N_2Cl$, 296.0200; found, 296.0201.

Study of PEtG 4 Degradation in Solution (General Procedure for the Study of Polymer Degradation). PEtG **4** (15 mg) was dissolved into a 9:1 mixture of CD_3CN:D_2O (1.2 mL) at ambient temperature (21 °C). The solution was then transferred into two NMR tubes, and the tubes were promptly sealed. One tube was exposed to UV light (wavelength: 300−350 nm, 5.3 mW cm^{-2}) to initiate the removal of the photolabile end-cap, and the absorbance at 340 nm was monitored by UV−vis spectroscopy to ensure the complete deprotection of the polymer (approximately 80 min). Another NMR tube was stored in a light-impermeable box over this time, and was prepared as a control for any background polymer degradation. ^{1}H NMR spectra then were recorded at defined intervals to monitor the depolymerization of the materials. At the same time, polymer **3** also underwent the same irradiation and NMR study, serving as a nontriggerable control. This same protocol was also applied to study the degradation of polymers **11**−**15** and **21**.

Mass Loss and SEC Degradation Study of PEtG 4 Films. PEtG **4** (3.0 g) was dissolved in CH_2Cl_2 (15 mL) and drop-cast onto 60 individual glass slides to provide films. After the solvent was evaporated in vacuo for 48 h in a desiccator, the mass of each film was recorded. Thirty films were placed into a UV box as described above for 17 h to remove the end-cap. During this time, the remaining slides were stored in the dark. Next, all of the slides were placed into a phosphate buffer solution (100 mM, pH = 7.4) at ambient

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temperature (21 °C). At selected times, three plates from each treatment were removed from the buffer solution, rinsed, and dried under house vacuum for 48 h and then weighed. After each set of samples was weighed, 5.0 mg from one slide of each treatment was analyzed by SEC.

■ ASSOCIATED CONTENT

Supporting Information

Additional experimental procedures, ^{1}H and ^{13}C NMR spectra, SEC chromatograms, M_n's determined by NMR, UV−vis spectra, TGA, and DSC data, and additional polyglyoxylate and micelle degradation studies. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

egillie@uwo.ca

Notes

The authors declare no competing financial interest.

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