

Organocatalytic Ring-Opening Polymerization of Trimethylene Carbonate To Yield a Biodegradable Polycarbonate

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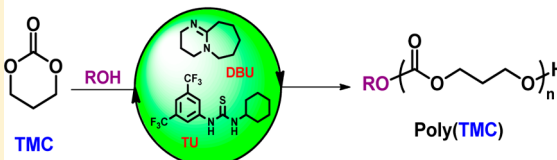
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S Supporting Information

ABSTRACT: In this laboratory experiment, students work in pairs to synthesize a simple aliphatic polycarbonate via ring-opening polymerization of trimethylene carbonate using 1,8-diazabicyclo[5.4.0]undec-7-ene and thiourea as organocatalysts. Following polymer isolation, students cool the material in a dry ice/acetone bath to observe its glass-transition behavior. This experiment is convenient to perform under teaching laboratory conditions and reinforces key concepts learned in second-year undergraduate organic chemistry, for example, nucleophilic acyl substitution, transesterification reactions, and Lewis acidity–basicity. Additionally, the experiment introduces students to polymer chemistry, heterocycles, materials science, and green chemistry. It also covers interesting concepts that are less frequently encountered at the undergraduate level such as biomimetic chemistry, bifunctional catalysis, and polymer–glass transitions.

KEYWORDS: Second-Year Undergraduate, Laboratory Instruction, Organic Chemistry, Polymer Chemistry, Hands-On Learning/Manipulatives, Catalysis, Lewis Acids/Bases, Nucleophilic Substitution, Polymerization, Materials Science

Organocatalytic Ring-Opening Polymerization



Polymers are widely found in both the natural world and modern society. Natural examples include biopolymers such as cellulose, proteins, DNA, and spider's silk, while examples of synthetic polymers include commodity plastics, synthetic fabrics and rubbers, etc. Despite this ubiquity and the fact that polymer science has grown into a major research area in both industry and academia, the topic remains under-represented in undergraduate chemistry^{1,2} and chemical engineering³ curricula. This issue has begun to be addressed, as evidenced by several recent publications that feature undergraduate polymer experiments.^{4–11} The current work contributes to this effort by providing a laboratory experiment on a class of polymers (i.e., polycarbonates) that has yet to be treated in this Journal. In addition, this laboratory exercise also demonstrates the phenomenon of polymer–glass transitions, a concept that has not been previously covered. This practical demonstration is visually appealing to students and simultaneously aids understanding and promotes enthusiasm in the topic. The pedagogical goals of this experiment are to introduce students to polymer chemistry, bifunctional catalysis, and green chemistry while many key concepts encountered in undergraduate organic chemistry, for example, nucleophilic acyl substitution, transesterification reactions, and Lewis acidity/basicity, are reinforced. Finally, this laboratory also illustrates the importance of NMR spectroscopy as a tool for monitoring reaction progress and analyzing polymer composition (e.g., to

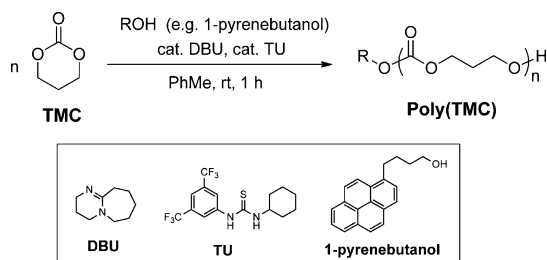
determine degree of polymerization, end group analysis, etc.) in addition to its routine use as a characterization method.

■ BACKGROUND

Aliphatic polycarbonates represent a class of polymers that are promising as biomaterials because of their biodegradability,¹² biocompatibility, and low toxicity. Earlier studies have shown that aliphatic polycarbonates undergo slow hydrolytic degradation in vitro and accelerated enzymatic degradation in vivo.^{12a} For instance, a poly(trimethylene carbonate) film incurred a 9% weight loss over 30 weeks via in vitro hydrolytic degradation, whereas the weight loss in rats over 24 weeks was 21.1%.^{12a} The degradation products of polycarbonates are alcohols and carbon dioxide. Potential applications of these polymers include drug delivery, gene delivery, and use as antimicrobial agents.^{13–17} Aliphatic polycarbonates can be synthesized by chain growth ring-opening polymerization (commonly abbreviated as ROP) of cyclic carbonates via organocatalytic, anionic, cationic, coordination–insertion, or enzymatic methods.^{18–20} Tin(II) bis(2-ethylhexanoate), or Sn(Oct)₂, is an effective and commonly used catalyst-initiator for ROP.^{4,9} However, the toxicity of tin compounds^{21–24} and the difficulty in removing heavy metal residues from polymer products stimulated the search for more environmentally-friendly catalysts.^{18–20} The

development of basic organocatalysts such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) has obviated the need for tin-based for ROP catalysts.^{18,25–27} By using a primary alcohol initiator such as 1-pyrenebutanol, polymerization of a cyclic carbonate such as trimethylene carbonate (TMC) can be readily initiated by catalytic quantities of DBU and a cocatalyst such as *N*'-[3,5-bis(trifluoromethyl)phenyl]-*N*-cyclohexylthiourea (TU) (Scheme 1). In just 1 h, high conversions of the

Scheme 1. Poly(TMC) Formed by Organocatalytic ROP of TMC



monomer to polycarbonate can be achieved. The short reaction time and robustness of the polymerization make this experiment ideal as a single-session laboratory experiment under standard teaching laboratory conditions. The absence of any toxic-metal catalysts is also attractive from a safety standpoint.

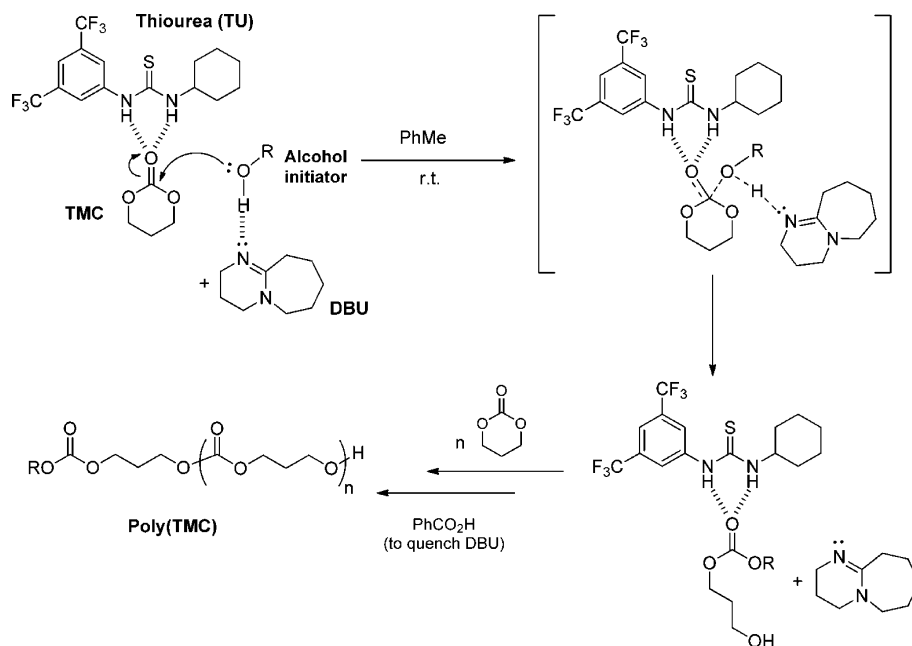
The putative polymerization mechanism²⁸ (Scheme 2) is particularly instructive for undergraduates as it involves many organic chemistry concepts such as nucleophilic substitution, tetrahedral intermediates, Lewis acids/bases, hydrogen bonding, and ring strain. Here, a dual-activation mechanism is operative. An alcohol initiator is activated by DBU, while the electrophilic carbonyl group of the monomer is activated by thiourea via hydrogen bonding in both cases. This is an example of bifunctional catalysis. The alcohol then attacks the carbonate in a nucleophilic acyl-substitution reaction whereby

the OH nucleophile first adds to the C=O of the carbonate to give a hydrogen-bonded tetrahedral intermediate that subsequently collapses to a linear hydroxyalkylcarbonate (Scheme 2). This hydrogen-bonded alcohol subsequently attacks another TMC molecule, and the entire process is repeated, which results in chain elongation. The terminal hydrogen-bonded alcohol becomes “dormant” when all monomer molecules are exhausted but resumes the chain-growth process if more TMC is subsequently introduced. Such a chain-growth polymerization mechanism, in which the polymer cannot undergo chain transfer or termination, is termed “living chain-growth polymerization”. When desired, the reaction is terminated by protonation, and hence removal of the DBU catalyst with an acid (e.g., benzoic acid), or by end-capping the terminal alcohol with acetyl chloride or acetic anhydride, occurs.

Living chain-growth polymerization enables precise control of the degree of polymerization (DP), dispersity (\bar{D}), and end-group fidelity. Dispersity, which reflects the distribution of molecular weights in a polymer sample, is another new concept to undergraduates without prior exposure to polymer chemistry. With organocatalytic ROP, it is possible to prepare narrow-disperse polycarbonate of any target DP by simply controlling the monomer-to-initiator feed ratio. In comparison, step-growth condensation polymerization limits the practically accessible range of polymer molecular weights and is typically associated with broader \bar{D} values. The ability to obtain narrow dispersities consistently can help to minimize batch-to-batch variations in the polymer’s physical or biological properties.

In this experiment, students are also introduced to the concept of glass transitions. The glass transition temperature (T_g) of a polymer is the temperature below which the material undergoes a transition from a soft, rubbery solid to a hard, glassy, and brittle one. The aliphatic polycarbonate featured in this laboratory has a T_g value of about $-30\text{ }^\circ\text{C}$. Following polymer isolation, students cool the material in a dry ice/acetone bath at $-78\text{ }^\circ\text{C}$ to induce this phase transition quickly, whereby the polycarbonate is transformed from a viscous syrup to a hard, glassy solid. Since the glass transition is reversible, the

Scheme 2. Formation of Poly(TMC) from TMC via a Dual-Activation Mechanism by DBU and TU



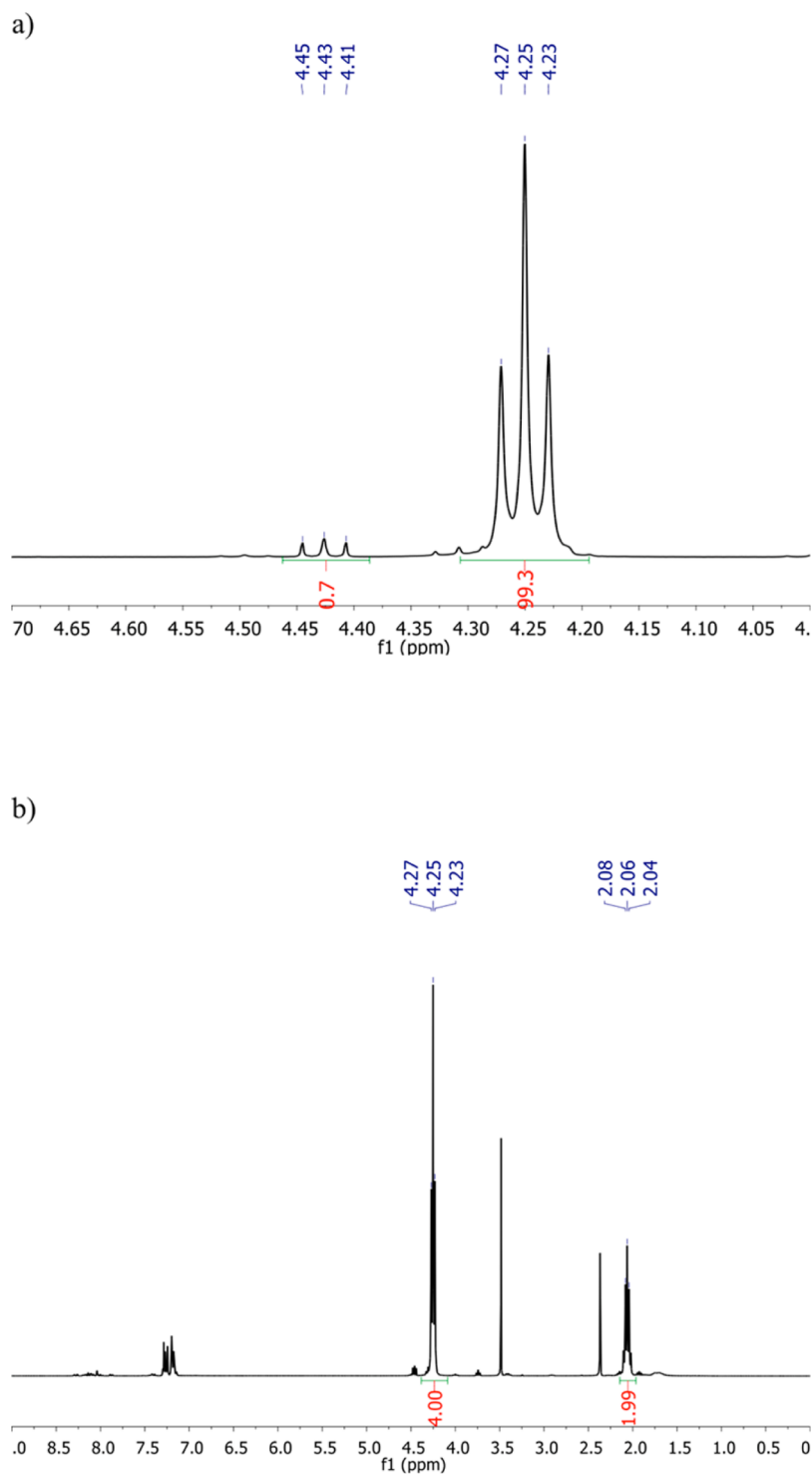


Figure 1. ^1H NMR (300 MHz) spectra. Crude sample: (a) expanded view of the 4.0–4.7 ppm region that shows 99% conversion, (b) full spectrum of precipitated poly(TMC). The use of ^1H NMR spectroscopy for polymer end-group analysis also allowed the average length of the polycarbonate chains, or the DP of the polymer, to be determined.

polymer reverts to its original state upon warming to room temperature. This final exercise is simple but of sufficient visual appeal to promote student enthusiasm, while it simultaneously introduces a physical chemistry concept.

EXPERIMENTAL SECTION

A single, 3 h laboratory session is required for this experiment, where students work in pairs to synthesize poly(TMC) via

organocatalytic ring-opening polymerization of TMC. In this experiment, TMC is dissolved in toluene with 1-pyrenebutanol (polymerization initiator) and a catalytic amount of the thiourea cocatalyst. In practice, any simple primary alcohol may be used, but in this case, the 1-pyrenebutyloxy moiety serves as a useful handle for characterization of the average DP by ^1H NMR spectroscopy or gel-permeation chromatography (GPC) in UV detection mode (where available). The basic

DBU catalyst is added last, and the mixture is stirred at room temperature for 1 h before being quenched with benzoic acid to bring about chain termination. A small quantity of the crude mixture is withdrawn by pipet for ^1H NMR spectroscopy so that monomer conversion to polymer can be determined. Students calculate the percentage conversion based on the relative signal integrations of the monomer versus polycarbonate methylene protons. The polycarbonate is precipitated into methanol, isolated, and air-dried. The vial containing the dry polymer is cooled to $-78\text{ }^\circ\text{C}$ in a dry ice/acetone bath to induce the liquid–glass transition, during which students observe a change in the material's physical appearance and mechanical properties. Finally, a second NMR sample (i.e., postpurification) of the polymer is prepared for determination of DP. Additional experimental details and accompanying instructor's notes are provided in the Supporting Information.

Laboratory Implementation

This polymer synthesis experiment was carried out by 12 students who worked in pairs as part of a second-year undergraduate organic chemistry laboratory course. The entire experiment was easily completed in about 3 h, and each student pair successfully synthesized, purified, and isolated the polycarbonate product under teaching laboratory conditions without the need for glovebox or Schlenk techniques.

Conversion of the TMC monomer to polycarbonate was evidenced by ^1H NMR spectroscopy since the four methylene protons proximal to the carbonate linkage show different chemical shifts (ppm) depending on whether they are on the cyclic carbonate monomer or the linear polycarbonate. The chemical shift of the four protons on TMC is 4.43 ppm, but as the ROP reaction progresses, a new triplet due to the methylene protons of poly(TMC) appears at 4.25 ppm (Figure 1). Percentage conversion of monomer-to-polymer was derived from the relative integrations of these two NMR peaks. Conversions achieved by the students ranged from 70% to nearly 100%, with two-thirds of the class obtaining over 90%. Figure 1 shows sample student NMR data that feature a crude spectrum before precipitation (expanded 4.0–4.7 ppm region) and a full spectrum of the precipitated polymer; the minor triplet at 4.30 ppm is from 1-pyrenebutanol. On the basis of the relative peak integrations in the crude NMR spectrum, these two students obtained a conversion of 99%.

The target DP value for this laboratory was 50, and most students successfully obtained values of about 35, while one student pair managed to achieve a DP value of 42. Gratifyingly, the ranges of experimental conversions (70–95%) and DP values (32–42) were fairly narrow across the board, and the deviations from expected values are most likely attributable to the accuracy with which the reagents and solvents were measured by the students.

The glass transition demonstration was observed by all students upon cooling of their isolated polymers in a dry ice/acetone bath. As the polymer was cooled below its glass transition temperature ($\approx -30\text{ }^\circ\text{C}$), the tacky, “gooey” polymer was transformed into a hard, glassy solid that could be picked up and manipulated with a spatula (Figure 2). On the basis of student feedback, this quick but visually stimulating demonstration was the most enjoyable part of the entire experiment; thus, this proved to be an easy yet effective way to visually illustrate the concept of a polymer–glass transition.

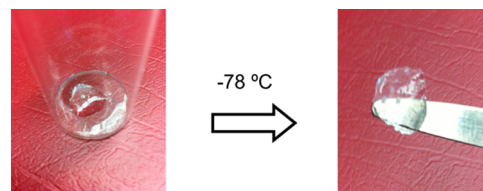


Figure 2. Liquid–glass transition of poly(TMC) induced by external cooling.

Possible Variations

Where available, GPC may be used to determine the number-average molecular weight (M_n) and the dispersity (M_w/M_n , where M_w is the weight-average molecular weight). Instrument access and circumstances permitting, students may submit their precipitated polymer samples for GPC analysis. The characterization would be carried out by the instructors after the laboratory session. This technique allows students to observe the molecular weight distribution of their polymers, something that is unattainable with NMR data alone.

HAZARDS

TMC, or 1,3-dioxan-2-one, is an irritant and may be harmful if inhaled or absorbed through the skin. Toluene, methanol, and acetone are flammable solvents that are harmful if swallowed and should be used in well-ventilated areas away from ignition sources. DBU is toxic if ingested and is a corrosive irritant to the skin and eyes. *N'*-[3,5-Bis(trifluoromethyl)phenyl]-*N*-cyclohexylthiourea (TU), 1-pyrenebutanol, and benzoic acid are irritants to the eyes, skin, and respiratory system. Dry-ice (solid CO_2) presents an asphyxiation hazard and may also cause cryogenic burns. Good ventilation is essential, and contact with exposed skin must be avoided. Chloroform-*d* is an inhalation hazard and suspected carcinogen. The poly(TMC) product should be assumed to be an irritant and handled as such. Students must wear safety glasses, face protection, protective clothing, and the appropriate gloves. All work should be carried out in well-ventilated fume hoods under the supervision of one or more instructors.

SUMMARY

This laboratory experiment on polycarbonate synthesis provided students the experience of synthesizing a simple biodegradable polymer and introduced them to the concepts of living chain-growth polymerization, ring-opening polymerization of a cyclic monomer, bifunctional catalysis, organo-catalysis, and glass transitions. The experiment was found to be highly reliable, with results being easily reproduced in 3 h or less by second-year organic chemistry undergraduates who worked in pairs under standard teaching laboratory conditions. Every student pair was successful in synthesizing a polymer, with two-thirds of the class achieving over 90% monomer conversion and the remainder obtaining around 70%. Most of the students obtained a polycarbonate with a DP value around 35, while one pair managed to achieve a DP value of 42. The range of student results in terms of conversion and DP value was fairly small, and the differences were ultimately attributed to how accurately the reagents and solvents were measured by the students. All students were able to observe the glass-transition behavior upon cooling of their isolated polymers.

The polymer experiment served to reinforce many of the principles that students had learned in their organic chemistry

classes. Furthermore, the simplicity, reproducibility, and visual appeal of the experiment enabled students to gain their first hands-on experience with polymer synthesis in an accessible, safe, and enjoyable way.

■ ASSOCIATED CONTENT

§ Supporting Information

Student handout, notes and detailed experimental procedure for instructors, list of chemicals, idealized NMR and GPC data obtained by the authors, and prelab and postlab questions and solutions. This material is available via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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