Surface-Accessible Detection Units in Self-Immolative Polymers Enable Translation of Selective Molecular Detection Events into Amplified Responses in Macroscopic, Solid-State Plastics

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S *Supporting Information*

ABSTRACT: This Communication describes a strategy for incorporating detection units onto each repeating unit of self-immolative CD$_r$ polymers. This strategy enables macroscopic plastics to respond quickly to specific applied molecular signals that react with the plastic at the solid–liquid interface between the plastic and surrounding fluid. The response is a signal-induced depolymerization reaction that is continuous and complete from the site of the reacted detection unit to the end of the polymer. Thus, this strategy retains the ability of CD$_r$ polymers to provide amplified responses via depolymerization while simultaneously enhancing the rate of response of CD$_r$-based macroscopic plastics to specific applied signals. Depolymerizable poly(benzyl ethers) were used to demonstrate the strategy and now are capable of depolymerizing in the context of rigid, solid-state polymeric materials.

Macroscopic stimuli-responsive materials could benefit substantially from the ability to self-amplify a macroscopic response to a specific molecular-level input. An amplified macroscopic response would allow a material to change its global properties in response to a local signal, increase the rate of change in the material, and decrease the quantity of signal necessary to induce the response.[1] One emerging strategy for realizing these benefits is based on self-immolative CD$_r$ polymers that are defined as having the capability of <u>c</u>ontinuous and complete <u>d</u>epolymerization when a molecular signal cleaves a detection unit (or end-cap) from the terminus of the polymer through a <u>r</u>eaction-based detection event. The reaction-based detection event provides selectivity for the response, while the continuous depolymerization reaction provides amplification.[2] Depolymerization of this type, however, suffers from slow rates of reaction between the applied molecular signal and the detection units that are displayed at the interface between a solid, macroscopic material and a surrounding liquid that contains the signal.[2i,3] In most cases, the detection unit constitutes <1% of the number of atoms in a polymeric material; therefore, few detection units statistically are accessible at the solid–liquid interface. Thus, the detection event has become the rate-limiting step in responses of CD$_r$-based macroscopic materials.

To ameliorate this rate-limiting step, we have now developed a strategy for substantially enhancing the number of detection units that are displayed at a solid–liquid interface by incorporating a detection unit onto each repeating unit of the CD$_r$ polymer that makes up the material.[4] This approach retains the ability to provide amplified responses via continuous and complete depolymerization, while also increasing the rate of the detection event.

We demonstrate this concept using a new type of depolymerizable poly(benzyl ether) (Figure 1b). First generation CD$_r$ poly(benzyl ethers) are not capable of depolymerizing in the solid state,[8] but poly(benzyl ethers) of the type depicted in Figure 1b depolymerize quickly in the solid state, which is a rare capability among CD$_r$ polymers (i.e., only poly(phthalaldehyde)[9] and poly(4,5-dichlorophthalaldehyde)[10] depolymerize on the macroscale in the context of solid-state plastics). These new poly(benzyl ethers) are more stable than poly(phthalaldehydes); therefore, they likely will become the preferred reagents in future studies for creating advanced stimuli-responsive materials with the capability of selective and amplified responses.

We prepared this new class of poly(benzyl ethers) using a short synthesis (3 steps, ~30% overall yield) to access quinone methide monomers that contain pendant detection units (Figure 2). In theory, a variety of detection units can be incorporated into these monomers,[2c] including proof-of-concept units that are responsive to Pd(0) (**4-allyl**, R$_1$ = allyl) or fluoride (**4-TBS**, R$_1$ = TBS). Polymerization of the monomers under anionic conditions (Figure 2) followed by end-capping provides access to polymers with detection units on each repeating unit (e.g., **5** and **8**), as well as control polymers either with detection units only on their termini (**6** and **9**) or without detection units (**7** and **10**).

As designed, polymers **5** and **6** depolymerize completely when they are dissolved in THF and exposed to excess fluoride (tetrabutylammonium fluoride; TBAF) at 23 °C (Figure S2). In contrast, control polymer **7** does not depolymerize, since it does not contain a TBS detection unit. LCMS analysis of aliquots of the depolymerization reaction of **5** with fluoride reveals deprotected and deprotonated quinone methide (i.e., **4-O⁻**, which we confirmed by LCMS (Figure S4) and via comparison with **4-O⁻** prepared by independent synthesis; Scheme S10)[11] as well as TBS-protected monomer **4-TBS** (where R$_1$ = TBS) (Figure S4). The presence of **4-TBS** confirms that depolymerization occurs via a head-to-tail amplification reaction, rather than via cleavage of every TBS group in the polymer. Similar results in terms of selective
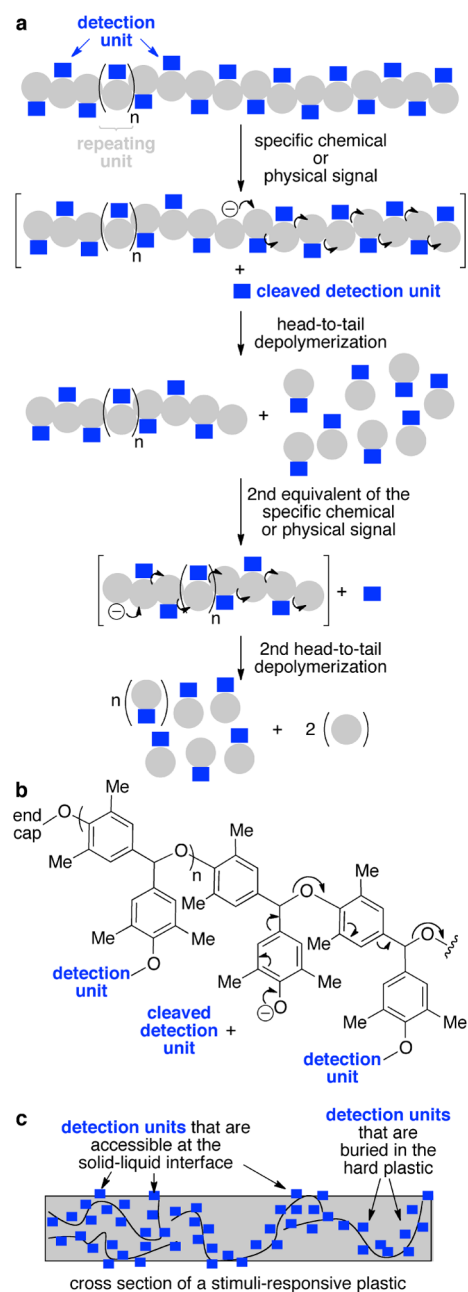
Figure 1. Strategy for creating stimuli-responsive rigid plastics that display amplified responses to specific signals at the solid−liquid interface. (a) Representation of the general design of the polymers in this study. (b) Specific backbone structure of the polymers used in this study. (c) Depiction of the challenge of placing detection units at the solid−liquid interface between a rigid plastic and its surroundings.
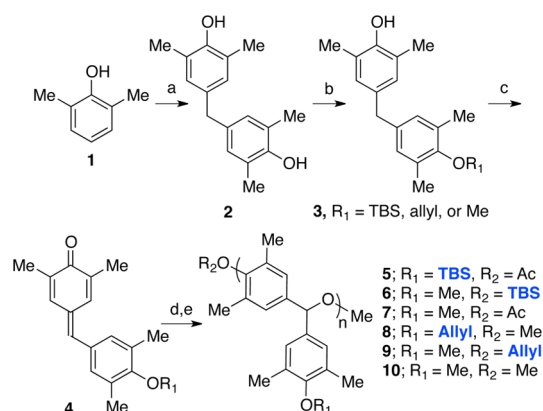

Figure 2. Preparation of monomers and polymers used in this study. Reagents and conditions: (a) formaldehyde, HCl (80%); (b) electrophile, base (to append R_1) (~50%); (c) Ag$_2$O (75%−80%); (d) MeOH, P$_2$-tBu; (e) electrophile, base (to append R_2) (31−89%). The detection units are highlighted in blue.

that the disks were rigid plastics rather than elastic materials. This rigidity is an important property when comparing the accessibility of detection units between disks made from different polymers.[12] In addition, disks made from **5** and **8** did not swell when submerged for 5 h in acetonitrile (the solvent used for the solid state depolymerization experiments) (Figure S6), which demonstrates that the disks do not substantially absorb the surrounding solvent that contains the molecular signal, and therefore the depolymerization experiments likely represent reactions at the solid−liquid interface. Moreover, spin-cast films of polymers **6−10** have nearly equal contact angles (e.g., 22° ± 1° for **7**) when wet with acetonitrile, while a film of polymer **5** is slightly higher (i.e., 35° ± 2°) (Figure S8). These results demonstrate that surfaces of solid-state objects made from each polymer will wet essentially equally with the fluid that contains the molecular signal; therefore, differences in wettability will not affect the response rates of the plastics to the applied molecular signals. Finally, scanning electron microscope (SEM) images of disks comprising polymers **5−7** show comparable surface morphology (Figure S7), further supporting the expectation that solid−liquid interactions will be similar across disks made from different polymers.

In the solid-state experiments, disks **5−7** were submerged in a nonstirring solution of acetonitrile containing 0.23 M TBAF at 23 °C and photographs were acquired over time (Figure 3). The disk made from polymer **5** responded in minutes by producing a deep purple color (from **11**)[13] and reducing in size (Figure 3a). In less than 5 h, the entire disk was converted into soluble products. In contrast to the rapid reaction of the disk made from **5**, the disk made from polymer **6** showed only minimal production of a yellow/blue color within the first 2 h of exposure to fluoride (presumably due to the few surface-accessible detection units), after which no additional reaction occurred (Figure 3b). In fact, after 7 days of exposure to fluoride, the disk appeared equal in size to its starting point. Likewise, the disk made from polymer **7** showed no change over 7 days of exposure to fluoride (Figure 3c).

These solid-state changes in morphology are corroborated by X-ray photoelectron spectroscopy analysis of solids made from polymers **5** and **6**. As anticipated, solids made from **5** contain 86% more silicon in the top 5 nm of the material than solids made from polymer **6**.[14]
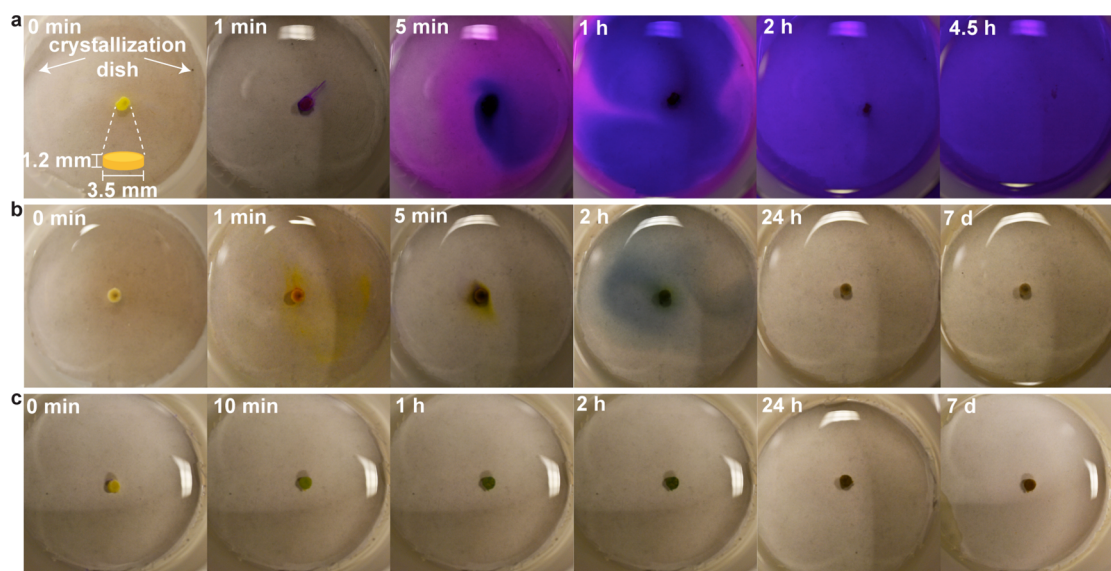
depolymerization were observed when polymers **8**, **9**, and **10** were exposed to Pd(0) in THF (Figure S3), thus confirming that the detection units can be changed on each repeating unit to alter the signal to which the polymer responds.

Depolymerization experiments in the solid state revealed substantial differences in the accessibility of detection units at the solid−liquid interface. Solid disks of polymers **5−10** were prepared by solvent casting each polymer into a silicon mold. Each disk was approximately 3.5 mm in diameter × 1.2 mm thick, weighing 10.2 mg ± 1.2 mg. Young's modulus values for two representative disks (made from **5** and **8**) ranged from 1.20 ± 0.06 GPa (for **5**) to 1.67 ± 0.11 GPa (for **8**), establishing

Figure 3. Photographs showing selective depolymerization at the solid−liquid interface using solvent-cast disks of polymers **5**−**7**. All photographs show a top-down view of a glass crystallization dish that contains a plastic disk immersed in a solution of acetonitrile that contains 0.23 M TBAF. The disk in (a) comprises polymer **5**, in (b) polymer **6**, and in (c) polymer **7**. Similar results are available in Figure S5 for disks made using polymers **8**−**10** that respond to Pd(0).

Similar selectivity in the solid-state depolymerization results were obtained for disks made from polymers **8**−**10** that respond to Pd(0) (Figure S5), showing that inclusion of detection units on each repeating unit of the poly(benzyl ethers) indeed accelerates the rate of molecular detection events at the solid−liquid interfaces of macroscopic poly(benzyl ether)-based materials.

The combination of these capabilities—i.e., tunable specificity, signal amplification, stimuli responses in rigid plastics, and rapid responses at solid−liquid interfaces—allows us to envisage applications of such materials. Example applications may range from plastics that easily alter their size, shape, structure, surface properties, or function to plastics that report their exposure to a specific analyte (via the purple color of **11**), to plastics that form the basis for smart capsules.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Procedures, figures, NMR spectra, and GPC chromatograms. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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(11) An independent synthesis was used to confirm the structure of **11** (see the Supporting Information).

(12) Under the same experimental conditions, Young's modulus value was obtained for poly(styrene) (2.87 ± 0.09 GPa) to provide internal comparison for our measurements of **5** and **8**. Literature values for poly(styrene) range from 3 to 3.6 GPa. Poly(propylene) has Young's modulus values that are similar to those for polymers **5** and **8** (i.e., 1.5−2 GPa).

(13) Quinone methide **11** is bright purple when deprotonated (λ_{max} = 574 nm; $\varepsilon = 1.4 \times 10^5 \ M^{-1} \ cm^{-1}$ in MeCN containing 5 mM DBU). These data were obtained using **11** that was prepared via an independent synthesis (see the Supporting Information) (Figure S1) and thus serves as a colorimetric reporter for depolymerization.

(14) Solids made from **5** contain 7% ± 1% silicon in the top 5 nm of the material, whereas solids from **6** contain 1% silicon.