Polymer Chemistry

Polymer Chemistry

PAPER

End-capped poly(4,5-dichlorophthalaldehyde): A stable self-immolative poly(aldehyde) for translating specific inputs into amplified outputs, both in solution and the solid state

Anthony M. DiLauro and Scott T. Phillips*

We recently reported that poly(4,5-dichlorophthalaldehyde) (PCl_2PA) is an effective self-immolative CD_r polymer for prototyping multi-stimuli-responsive three-dimensional polymeric materials with response properties that are inspired by the behaviour of certain biological materials in plants. In this article we [10] detail the design and synthesis of PCl_2PA, describe its ability to respond to specific stimuli, and compare and contrast PCl_2PA with poly(phthalaldehyde) (PPA), which is the self-immolative CD_r predecessor of this new poly(acetal). This article illustrates the favourable attributes of PCl_2PA, including its dose-dependent solution-phase response to Pd(0). Taken together, these studies reveal the unique and useful attributes of PCl_2PA for providing selective amplified responses to specific stimuli, both in solution and [15] the solid state.

Introduction

Poly(phthalaldehyde) (PPA) was first reported in 1967[1] and was subsequently explored as a candidate photoresist for photolithography 16 years later.[2] In this context, the polymer [20] depolymerizes quickly and completely at room temperature (presumably via random cleavage of acetal linkages along the polymer backbone) when exposed to a photoacid that is generated from exposure of ultraviolet light to a photoacid generator.[2,3] Unfortunately, this depolymerization reaction occurred directly in [25] the exposure tool, which led to coating of the expensive optics of the instrument, and discontinued use of the polymer for photolithographic applications.[4]

Forty-three years after the initial preparation of PPA, the polymer re-emerged in the form of PPA derivatives that were [30] end-capped with either one or two reaction-based detection units.[5] These reaction-based detection units are functionalities that provide selective responses to PPA by dictating the specific chemical or physical signals that cause end-to-end depolymerization (Fig. 1a). Rather than depolymerizing as a [35] result of random cleavage of the polymer backbone (e.g., Fig. 1c), the resulting un-end-capped terminus of the polymer (i.e., a hemiacetal) causes the polymer to quickly revert to monomers due to the low ceiling temperature of the un-end-capped polymer (–40 °C).[5a] This ability to impart selective and amplified [40] responses (via **c**ontinuous **d**epolymerization after a single **r**eaction-based detection event; hence the CD_r nomenclature) has led to a variety of new applications for PPA, including shape-changing plastics;[5a,c] stimuli-responsive core-shell microcapsules;[5d] and microscale, non-mechanical stimuli-

[45] responsive pumps,[5b,e] all of which are capable of translating a molecular detection event into an amplified, macroscopic response in a material. PPA also has been applied recently as a resist in thermal probe lithography;[6] as a thermally responsive material;[7] as self-assembled materials;[8] as mechanoresponsive [50] polymers;[9] as a nanochannel template;[10] and as cyclic polymers (that lack detection units),[11] which are being developed as a degradable substrate for transient electronics,[12] graphene transfer,[13] and as reconfigurable polymers.[14] Thus, over the past five years, PPA has quickly become a privileged polymer due to [55] its ability to provide an amplified response both in solution and the solid state. Despite its unique role in enabling these new applications, PPA has one undesirable attribute that severely limits its further application: the poly(acetal) backbone of the polymer is sensitive to mild acid and is unstable even when [60] stored as a solution or as a solid at 23 °C,[15] thus giving rise to undesirable background depolymerization.

To overcome these stability issues, while still maintaining the favourable properties of PPA, we designed poly(4,5-dichlorophthalaldehyde) (PCl_2PA).[16] Herein we describe the full [65] development of PCl_2PA, including its design, synthesis, stability, and ability to provide amplified responses to specific signals. Based on the results of these studies, we believe that PCl_2PA will quickly replace PPA as a privileged reagent for creating new types of smart engineered materials that display selective, [70] dynamic, and amplified responses, and that are capable of translating a specific molecular detection event into a macroscopic response in a material.

Polymer Chemistry Accepted Manuscript
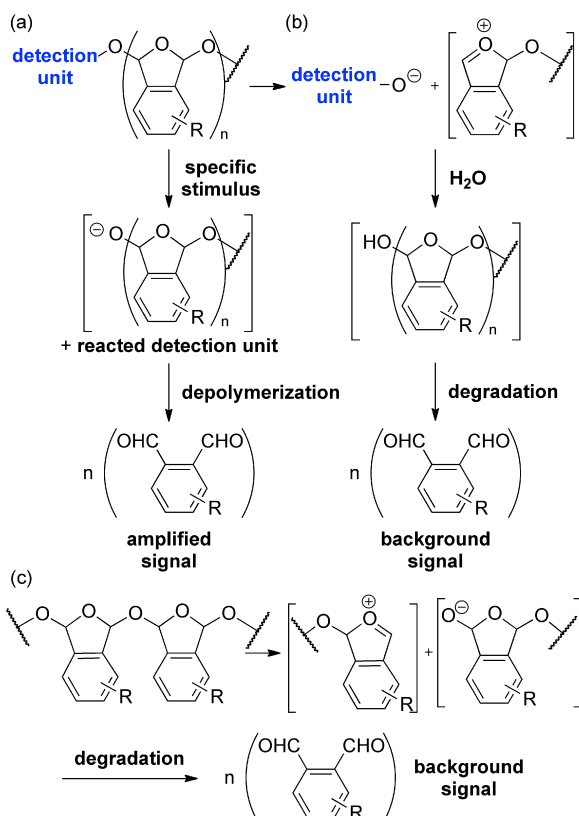
Fig. 1 Proposed pathways leading to depolymerization of poly(phthalaldehydes) that contain reaction-based detection units (i.e., end-caps): (a) Desired pathway where the detection unit is cleaved selectively in the presence of an applied signal.[5a] (b), (c) Two possible mechanisms for non-specific degradation of the polymer, the former from heterolytic cleavage of the detection unit and the latter from heterolytic cleavage of the polymer backbone.

Results and Discussion

Design of PCl₂PA.

We predicted that background degradation in PPA may arise from non-specific cleavage of either the end-cap (Fig. 1b) or the polymer backbone (Fig. 1c), or a combination of the two mechanisms. Both mechanisms would, in principle, reveal polymer chains without end-caps and cause unwanted depolymerization and background signal. We hypothesized that we could improve the stability of end-capped poly(phthalaldehydes) by strategically placing electron withdrawing substituents on each repeating unit *para* to the acetals in the polymer backbone (i.e., two electron withdrawing groups per repeating unit; one *para* to each acetal on each side of the repeating unit).[16,17] This hypothesis led us to pursue 4,5-dichlorophthalaldehyde (**3**) as a candidate monomer that could be accessed more easily than the fluorinated analogue, while still retaining electron withdrawing character. We were reluctant to pursue monomers with stronger electron withdrawing groups, such as nitro groups, for reasons of safety, but also because strong electron withdrawing groups would increase the reactivity of the polymer and the monomer. For example, inclusion of two *para* nitro groups instead of chlorines would increase the acidity of the acetal hydrogen atoms at the benzylic positions of the polymer,[18] which could impart unwanted susceptibility of the

backbone to degradation under basic conditions. Similarly, with two *para* nitro groups, the dialdehyde monomer would be prone to hydration of the aldehydes,[19] which would severely complicate the purification procedure for accessing dry dialdehyde monomer for anionic polymerization. Thus, we settled on dichloro substitution as a compromise between these considerations.

Synthesis of end-capped PCl₂PA.

Our synthetic route for preparing 4,5-dichloro-1,2-benzenedicarboxaldehyde was recorded in the Supplementary Information of our recent paper on additive manufacturing of 3D, multi-stimuli-responsive polymers.[16] Here we describe the synthesis in detail and offer insight into accessing 1,2-benzene dialdehydes with the appropriate purity for anionic polymerization.

The synthetic route is depicted in Scheme 1 and involves oxidation of **2** to the corresponding dialdehyde. Only a few procedures have been reported for realizing this transformation to generate aromatic 1,2-dialdehydes,[20] therefore we optimized the reaction conditions using 1,2-benzenedimethanol (**4**) (Fig. 2) as an inexpensive and readily available test system. Fig. 2 reveals that Swern oxidation conditions gave nearly quantitative yield (by ^{1}H NMR) of the aromatic dialdehyde (**5**). 2-Iodoxybenzoic acid (IBX) was effective as well (entry 2), but nearly all other conditions that we explored gave poor yields of the 1,2-dialdehyde (**5**) and instead often provided the lactone (i.e., phthalide).
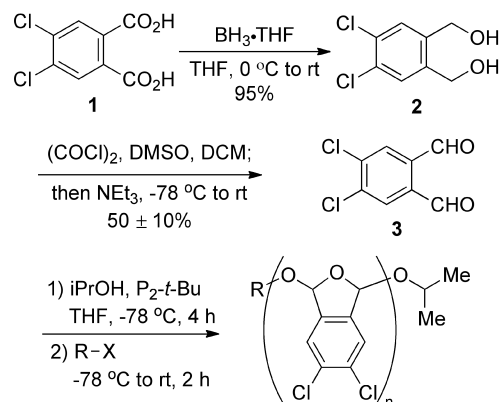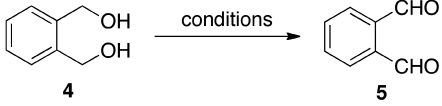

Scheme 1 Synthesis of 4,5-dichloro-1,2-benzenedicarboxaldehyde and the corresponding polymerization reaction to form end-capped PCl₂PA.[16] The yield for the oxidation of **2** to **3** is the average and standard deviation of nine experiments.

The reduced yield shown in the preparation of **3** (Scheme 1) relative to the anticipated value from the ^{1}H NMR data for **5** in Fig. 2 reveals the difficulty associated with isolating analytically pure aromatic 1,2-dialdehydes. In fact, in unpublished work we have encountered substantial difficulty in isolating various aromatic 1,2-dialdehydes. Thus, the procedure for isolating **3** is worth detailing, particularly since the purity of **3** is correlated with the success of the polymerization reaction in Scheme 1, as was previously observed in the synthesis of PPA.[5c]

Dialdehyde **3** can be isolated via flash column chromatography, but in our hands this procedure was not reproducible: sometimes it yielded the product and other times substantial degradation of the dialdehyde was observed. Instead

of using flash chromatography, we dissolve **3** in THF (triethylammonium salts remain insoluble) after concentrating the solvent from the Swern oxidation, remove the salts by filtration, evaporate the THF, and then vacuum sublime **3**. Recrystallization of **3** (twice) from chloroform provides **3** with sufficient purity to enable reproducible polymerization reactions, but also likely contributes to the reduced yield for the oxidation reaction.

Using anionic polymerization conditions,[16] PCl$_2$PA can be obtained in ~70% yields with polymer lengths ranging from 4 kDa to 40 kDa (M_n) (depending on the quantity of initiator used in the reaction) and PDI values of ~1.4.

entry	reagents	temp (°C)	^{1}H NMR yield (%)
1	(COCl)$_2$, DMSO, then Et$_3$N	−78	95
2	IBX	80	72
3	BaMnO$_4$	23	28
4	PDC	23	5
5	MnO$_2$	23	19
6	NaOCl, TEMPO, NaHCO$_3$, KBr, DCM, H$_2$O	10	1

Fig. 2 Conditions and ^{1}H NMR yields for the oxidation of 1,2-benzenedimethanol (**4**) to 1,2-benzenedicarboxaldehyde (**5**). 1,2-Benzenedimethanol was used as an inexpensive surrogate to optimize the oxidation of **2** to **3**.

Effect of electron withdrawing groups on the stability of PCl$_2$PA in neutral solutions.

We compared the stabilizing effect of chlorine substitution (e.g., PCl$_2$PA) versus hydrogen substitution (PPA) using six polymers that differed in the composition of the end-cap on the polymer. These derivatives were stored protected from light at 23 °C in THF-d_8 and were monitored over time by ^{1}H NMR for the appearance of monomer (Fig. 3).[21] The time-dependent concentration of monomer (determined by comparison of integration values to an internal standard) provided a measure of the extent of depolymerization of the various polymers.

These studies reveal that carbonate-linked end-capped polymers NVOC-PPA-OiPr (**6**) and Alloc-PPA-OiPr (**7**) (Fig. 4) degrade by 0.8−3.2% per day, with variation in the background degradation rate dictated by the composition of the carbonate end-cap (Fig. 4). In contrast, ester-linked end-capped polymer Ac-PPA-OiPr (**8**) showed negligible degradation under these conditions.

Electronic effects likely account for these differences in stability. For example, since PPA derivatives **6** and **7** are identical to one another with the exception of the composition of the carbonate end-caps, we reason that the difference in degradation rate between the two is the effect of leaving group ability of the

end-caps: the pK$_a$ (water) for allyl alcohol is 15.5[22] vs. ~13.6[23] for the substituted benzylic alcohol end cap in **6**. This difference in acidity is consistent with an electronic effect that likely translates into enhanced leaving group ability (via the postulated mechanism in Fig. 1b) for the carbonate end cap in **6** vs. the corresponding allyl carbonate end cap in **7**. Similarly, carbonate end caps are better leaving groups (via the mechanism in Fig. 1b) than esters, as would be expected based on pK$_a$ values (i.e., pK$_a$ (water) for carbonic acids $\cong$ 3, while pK$_a$ (water) for acetic acid is 4.76)[24,25].

While it may be possible to link some reactive detection units via an ester linkage, it is more common to link detection units to the end of the polymer through carbonates.[5a,c] Thus, these results confirm that a universal solution is needed to address the issue of background degradation in end-capped poly(phthalaldehydes). Towards this end, Fig. 4 further reveals that non-specific degradation can be prevented by incorporating electron withdrawing chlorine substituents *para* to the acetals in the polymers, even in derivatives with carbonates linking the polymer to the end-cap (e.g., **9** vs. **6**, and **10** vs. **7**).
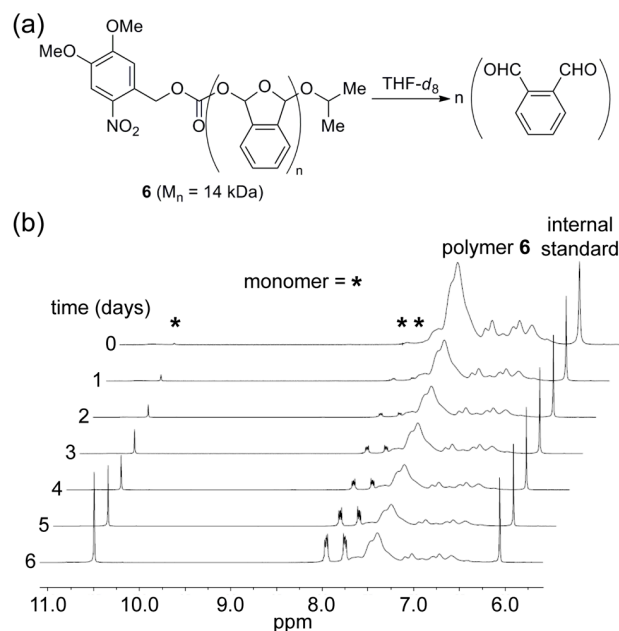

Fig. 3 Method for measuring the non-specific degradation of poly(phthalaldehydes). (a) A representative reaction sequence for the experiment. (b) ^{1}H NMR spectra of polymer **6** (M_n = 14 kDa) over a period of six days in the dark. Percent degradation was calculated from ^{1}H NMR integration values for the aldehyde peak of the monomer relative to an internal standard with a known concentration, and is equal to (moles of monomer)/(total possible moles of monomer at 100% degradation) × 100.

Effect of electron withdrawing groups on the stability of PCl$_2$PA when exposed to acid.

The stabilizing effect of chlorine substitution is more pronounced when the polymers are exposed to mild acid in THF than when exposed to pure THF. Specifically, exposure of the polymers to 100 equiv of BzOH[26] for 6 d in THF-d_8 (in the dark) revealed that Alloc-PPA-OiPr (**7**) and Ac-PPA-OiPr (**8**) degrade 30-fold more

per day under these conditions than either Alloc-PCl$_2$PA-OiPr (**10**) or Ac-PCl$_2$PA-OiPr (**11**) (Fig. 5). These results suggest that dichloro substitution stabilizes the polymer from undesired background reactions both at the end-cap and the polymer backbone, thus minimizing the effects of both pathways b and c in Fig. 1.
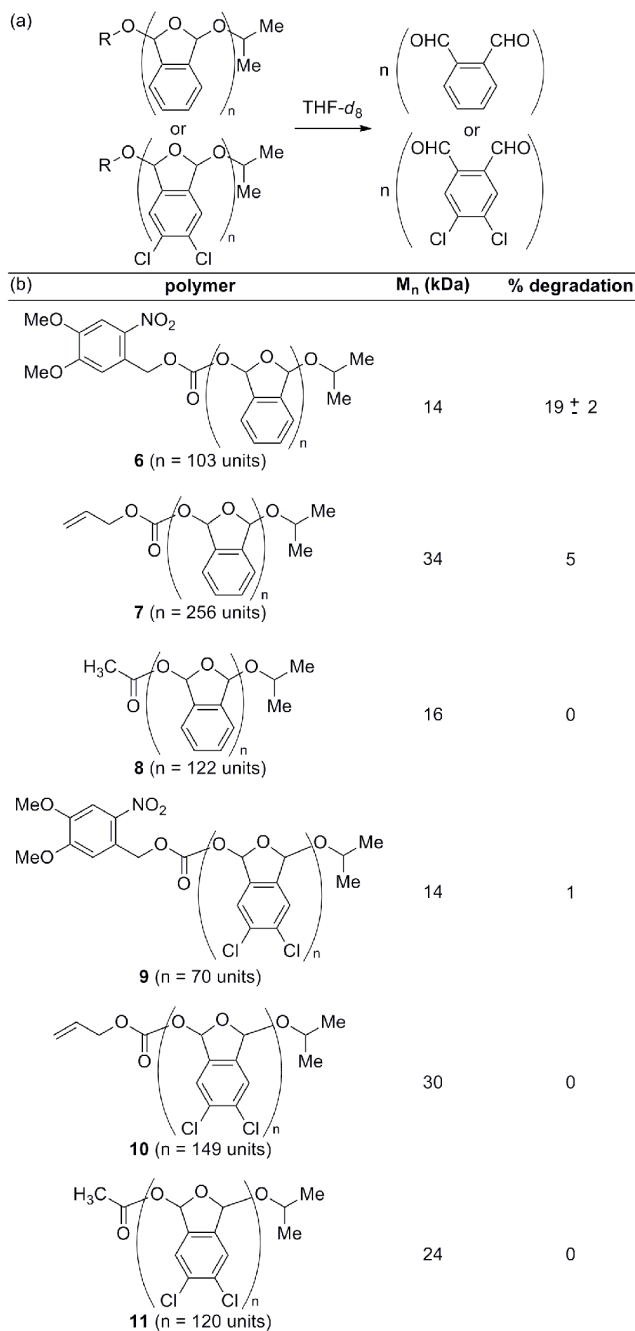
Fig. 4 Percent degradation of 7.0 mM solutions of polymers **6–11** after 6 d in the dark in THF-d_8. (a) The reaction conditions. (b) Table showing the percent degradation of the corresponding polymers. The percent degradation values were determined as outlined in Fig. 3. The data for polymer **6** is the average and standard deviation of three measurements.

Effect of electron withdrawing groups and end-caps on the thermal stability of PCl$_2$PA.

As mentioned in reference 16, thermal gravimetric analysis (TGA) measurements reveal that chlorine substitution also renders PCl$_2$PA more stable than PPA to degradation caused by heat. For example, Alloc-PCl$_2$PA-OiPr (**10**) is more stable than Alloc-PPA-OiPr (**7**) by approximately 40 °C (Fig. 6), as is Ac-PCl$_2$PA-OiPr (**11**) relative to Ac-PPA-OiPr (**8**). The data also support the observation that ester-linked end-caps are more stable (by approximately 10 °C) than carbonate linked end-caps.
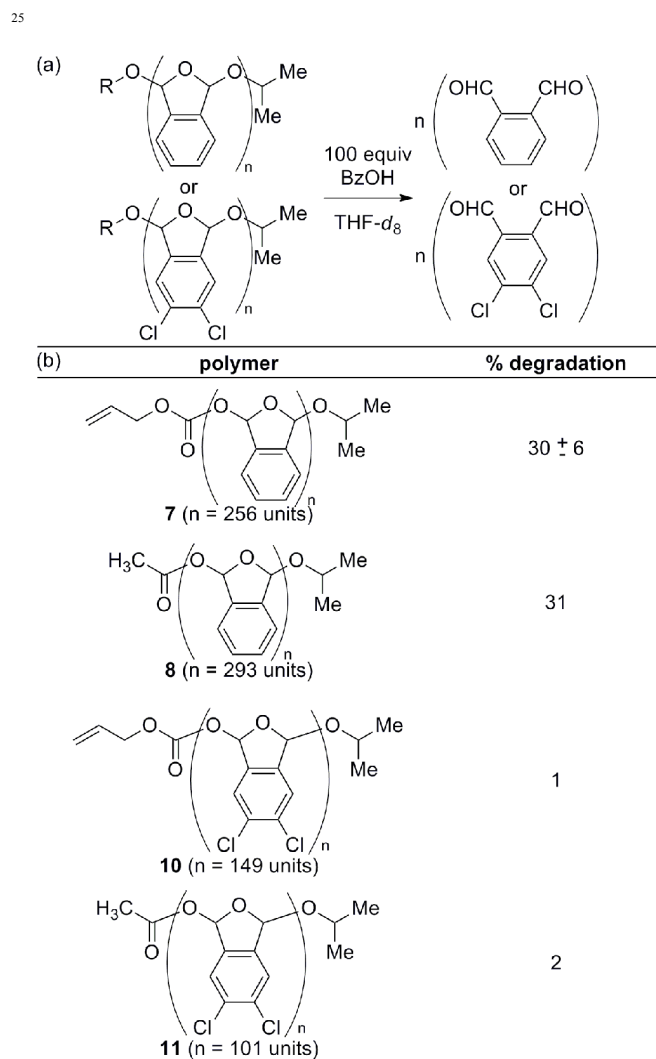
Fig. 5 Percent degradation of 5.2 mM solutions of polymers **7**, **8**, **10**, and **11** after 6 d in the presence of 100 equiv of BzOH in THF-d_8. (a) The reaction conditions. (b) Table showing the percent degradation of the corresponding polymers. The percent degradation values were calculated as defined in Fig. 3. The data from polymer **7** is the average and standard deviation of three measurements.

Selective depolymerization of PCl$_2$PA.

This increase in stability for PCl$_2$PA versus PPA does not prevent end-capped PCl$_2$PA from depolymerizing completely and continuously from end to end when exposed to a specific applied signal at room temperature, both in solution and in the solid state

(solid state demonstrations are provided in reference 16). This ability to depolymerize quickly in the solid state is particularly unique among the current classes of CD_r polymers[27] (with the exception of PPA), and should be useful in a variety of solid-state materials applications.


Fig. 6 Normalized TGA curves and thermal degradation temperatures for Alloc-PPA-O*i*Pr (**7**) (black), Ac-PPA-O*i*Pr (**8**) (orange), Alloc-PCl₂PA-O*i*Pr (**10**) (blue), and Ac-PCl₂PA-O*i*Pr (**11**) (pink). The data for polymer **10** in the corresponding table is the average and standard deviation of three measurements.
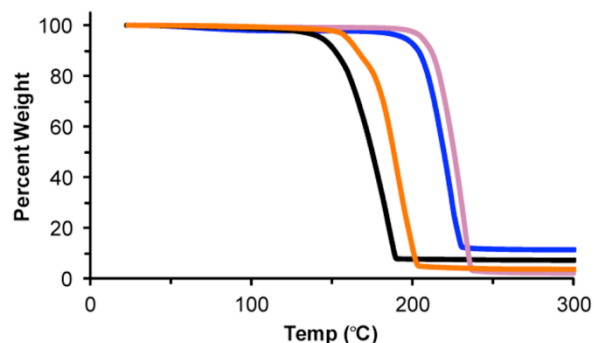
Polymer	M_n (kDa)	Onset Temp (°C)	Endset Temp (°C)
7	34	160	189
8	39	174	202
10	30	205 ± 2	230 ± 5
11	17	213	236

In solution, the depolymerization reaction is dependent on the dose of the specific applied signal. For example, when exposed to varying concentrations of Pd(0) for a fixed time (30 min), Alloc-PCl₂PA-O*i*Pr (**7**) provided a dose-dependent depolymerization response, as measured by ¹H NMR (Fig. 7). The curve that correlates extent of depolymerization as a function of the concentration of Pd(0) approaches a maximum value at approximately 1.2 mM Pd(0), where close to 100% of the polymer has depolymerized within the 30 min exposure period. As expected, the response is selective for the polymer end-capped with the responsive Alloc group: i.e., a similar experiment with Ac-PCl₂PA-O*i*Pr (**11**) and Pd(0) revealed no significant depolymerization (Fig. 7b).

These results suggest the potential for using the solution-phase depolymerization of CD_r polymers as a quantitative measure of analyte concentration, where the monomers produced via an analyte-induced depolymerization reaction are used as a direct signal of the detection event. In this context, the stability of the polymer is particularly important, since non-specific degradation of PCl₂PA would lead to background signal, decreased sensitivity, and/or irreproducible results.
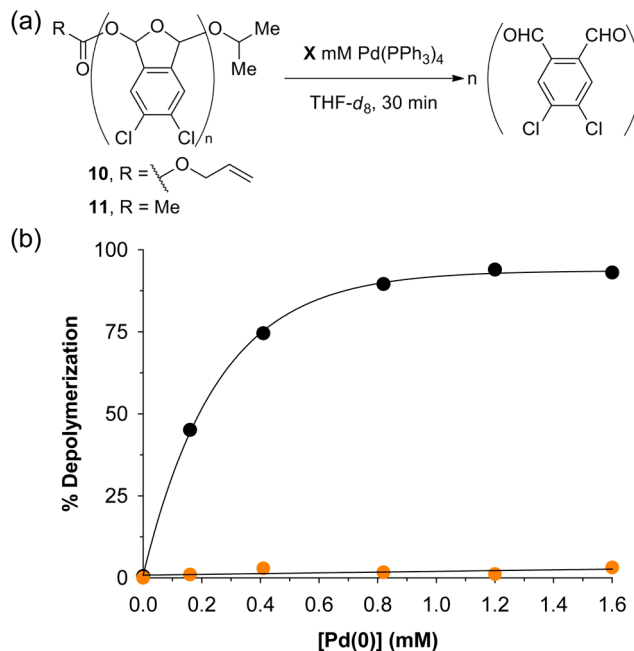
Fig. 7 Selective dose-dependent response of polymer **10** to Pd(0). (a) Conditions for evaluating the response of polymers **10** and **11** to different concentrations of Pd(0). (b) Percent depolymerization of polymers **10** (black) and **11** (orange) in the presence of different concentrations of Pd(0). Percent depolymerization was calculated using ¹H NMR values for the aldehyde peak of the monomer relative to an internal standard with a known concentration. Percent depolymerization is equal to (moles of monomer)/(total possible moles of monomer at 100% depolymerization) × 100. The lines are provided as visual aids.

Conclusions

Poly(phthalaldehyde) (PPA) emerged recently as a privileged polymer for imparting selective, rapid, and amplified responses to solid-state materials,[5–14] despite a high level of instability in the polymer backbone. PCl₂PA, as reported herein, retains all of the benefits of PPA, but overcomes many of its limitations. Thus, PCl₂PA should serve as an effective replacement for PPA, and thus should facilitate the rapid development of various types of stimuli-responsive materials with improved stability compared to materials made from PPA.

Experimental

General Experimental

All reactions were performed in flame-dried glassware under a positive pressure of argon unless otherwise noted. For polymerization reactions, glassware was flame-dried and stored in a glove box overnight, and argon was passed through an Agilent oxygen trap BOT-4. Air-and moisture-sensitive liquids were transferred by syringe or stainless steel cannula. Organic solutions were concentrated by rotary evaporation (25–40 mmHg) at ambient temperature, unless noted otherwise. All reagents used were purchased commercially and were used as received unless noted otherwise. 2-Iodoxybenzoic acid (IBX) was synthesized as described by Frigerio et al.[28] 1-[[(Chlorocarbonyl)oxy]methyl]-4,5-dimethoxy-2-nitrobenzene was synthesized as described by Katritzky et al.[29] 4,5-Dichlorophthalaldehyde (**3**) and polymers **9**–**12** were synthesized

as described in ref 16 and polymers **6–8** were synthesized as described in ref 5c. Dichloromethane and dimethylsulfoxide were purified by the method developed by Pangborn et al.[30] Thin layer chromatography was carried out on Dynamic Adsorbents silica gel TLC (20 × 20 cm w/h, F-254, 250 μm).

Instrumentation

Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 25 °C unless noted otherwise. Proton chemical shifts are express in parts per million (ppm, δ scale) and are referenced to tetramethylsilane $((CH_3)_4Si$, 0.00 ppm) or to residual protium in the solvent (THF-d_8, 3.58 ppm). Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and/or multiple resonances, br = broad peak), integration, and coupling constant (J) in hertz.

Gel permeation chromatography (GPC) analyses were performed using an Agilent Technologies 1200 GPC equipped with a refractive index detector, a Malvern Viscotek model 270 Dual Detector with right and low-angle light scattering, and either two Agilent Resipore columns (300 mm × 7.5 mm) in series or a single Agilent Resipore column (300 mm × 7.5 mm) using THF as the mobile phase (flow rate: 1 mL/min, 25 °C). The GPC was calibrated using monodisperse polystyrene standards from Malvern.

Thermal gravimetric analysis (TGA) was accomplished using a TA Instruments 2050 TGA. Scans were collected in the range of 25 °C to 300 °C with a ramping rate of 10 °C/min under a dry N_2 atmosphere.

Solution phase stability study

Solutions of polymers **6** (M_n = 14 kDa), **7** (M_n = 34 kDa), **8** (M_n = 16 kDa), **9** (M_n = 14 kDa), **10** (M_n = 30 kDa) and **11** (M_n = 24 kDa) (0.0035 mmol) with concentrations of 7.0 mM were prepared in THF-d_8 (0.5 mL)[21] that contained a known concentration of an internal standard (1,3,5-trimethoxybenzene). The polymer solutions were stored protected from light at 23 °C. After 6 d, the quantity of monomer in each solution was measured using ^{1}H NMR by comparing the integration values of the aldehyde peak of the monomer to the aromatic peak of the internal standard (Table S1). The experiment with polymer **6** was repeated three times.

Acid stability study

Polymers **7** (M_n = 34 kDa), **8** (M_n = 39 kDa), **10** (M_n = 30 kDa) and **11** (M_n = 21 kDa) (0.0026 mmol) were dissolved in THF-d_8 (0.5 mL)[21] that contained a known concentration of an internal standard (1,3,5-trimethoxybenzene) and 0.52 M benzoic acid (0.26 mmol, 100 equiv) to give 5.2 mM solutions of polymer. The polymer solutions were stored protected from light at 23 °C. After 6 d, the quantity of monomer in each solution was measured using ^{1}H NMR by comparing the integration values of the aldehyde peak of the monomer to the aromatic peak of the internal standard (Table S2). The experiment with polymer **6** was repeated three times.

Dose-dependent response of PCl$_2$PA to Pd(0)

To 1.8 mM solutions of polymers **10** (M_n = 30 kDa) and **11** (M_n = 20 kDa) in THF (0.5 mL solutions, 0.89 μmol polymer) was added 0.5 mL solutions containing varying concentrations of tetrakis(triphenylphosphine)palladium(0) (0 mM, 0.16 mM, 0.41 mM, 0.82 mM, 1.2 mM, or 1.6 mM). The resulting solutions were agitated by vortexing for 5 s and then left undisturbed for 30 min. Aliquots (0.25 mL) from the solutions were added to 0.25 mL of THF-d_8 that contained a known concentration of an internal standard (1,3,5-trimethoxybenzene). The extent of depolymerization was measured using peak integration values in ^{1}H NMR spectra (Tables S3 and S4).

Notes and references

Department of Chemistry, Pennsylvania State University, University Park, Pennsylvania 16802, United States. E-mail: sphillips@psu.edu
† Electronic Supplementary Information (ESI) available: Procedures and NMR spectra for the oxidation experiment; tables of primary data. See DOI: 10.1039/b000000x/

1 (a) C. Aso and S. Tagami, *J. Polym. Sci., Part B: Polym. Lett.,* 1967, **5**, 217–220. (b) C. Aso, S. Tagami and T. Kunitake, *J. Polym. Sci., Part A: Polym. Chem.,* 1969, **7**, 497–511.
2 H. Ito and C. G. Willson, *Polym. Eng. Sci.,* 1983, **23**, 1012–1018.
3 H. Ito, E. Flores and A. Renaldo, *J. Electrochem. Soc.,* 1988, **135**, 2328–2333.
4 (a) H. Ito, M. Ueda and R. Schwalm, *J. Vac. Sci. Technol., B*, 1988, **6**, 2259–2263. (b) H. Ito and R. Schwalm, *J. Electrochem. Soc.,* 1989, **136**, 241–245.
5 (a) W. Seo and S. T. Phillips, *J. Am. Chem. Soc.,* 2010, **132**, 9234–9235. (b) H. Zhang, K. Yeung, J. S. Robbins, R. A. Pavlick, M. Wu, R. Liu, A. Sen and S. T. Phillips, *Angew. Chem. Int. Ed. Engl.,* 2012, **51**, 2400–2404. (c) A. M. DiLauro, J. S. Robbins and S. T. Phillips, *Macromolecules,* 2013, **46**, 2963–2968. (d) A. M. DiLauro, A. Abbaspourrad, D. A. Weitz and S. T. Phillips, *Macromolecules,* 2013, **46**, 3309–3313. (e) A. M. DiLauro, H. Zhang, M. S. Baker, F. Wong, A. Sen and S. T. Phillips, *Macromolecules,* 2013, **46**, 7257–7265.
6 (a) O. Coulembier, A. Knoll, D. Pires, B. Gotsmann, U. Duerig, J. Frommer, R. D. Miller, P. Dubois and J. L. Hedrick, *Macromolecules,* 2010, **43**, 572–574. (b) A. W. Knoll, D. Pires, O. Coulembier, P. Dubois, J. L. Hedrick, J. Frommer and U. Duerig, *Adv. Mater.,* 2010, **22**, 3361–3365. (c) F. Holzner, C. Kuemin, P. Paul, J. L. Hedrick, H. Wolf, N. D. Spencer, U. Duerig and A. W. Knoll, *Nano Lett.,* 2011, **11**, 3957–3962. (d) L. L. Cheong, P. Paul, F. Holzner, M. Despont, D. J. Coady, J. L. Hedrick, R. Allen, A. W. Knoll and U. Duerig, *Nano Lett.,* 2013, **13**, 4485–4491. (e) J. De Winter, A. P. Dove, A. Knoll, P. Gerbaux, P. Dubois and O. Coulembier, *Polym. Chem.,* 2014, **5**, 706–711.
7 S. Köstler, B. Zechner and B. Trathnigg, *J. Polym. Sci., Part A: Polym. Chem.,* 2009, **47**, 1499–1509.
8 J. A. Kaitz, C. M. Possanza, Y. Song, C. E. Diesendruck, A. J. H. Spiering, E. W. Meijer and J. S. Moore, *Polym. Chem.,* 2014, **5**, 3788–3794.
9 (a) C. E. Diesendruck, G. I. Peterson, H. J. Kulik, J. A. Kaitz, B. D. Mar, P. A. May, S. R. White, T. J. Martinez, A. J. Boydston and J. S. Moore, *Nat. Chem.,* 2014, **6**, 623–628. (b) G. I. Peterson and A. J. Boydston, *Macromol. Rapid Commun.,* 2014, **35**, 1611–1614.
10 A. P. Vogt, J. De Winter, P. Krolla-Sidenstein, U. Geckle, O. Coulembier and C. Barner-Kowollik, *J. Mater. Chem. B,* 2014, **2**, 3578–3581.
11 J. A. Kaitz, C. E. Diesendruck and J. S. Moore, *J. Am. Chem. Soc.,* 2013, **135**, 12755–12761.

12 H. L. Hernandez, S.-K. Kang, O. P. Lee, S.-W. Hwang, J. A. Kaitz, B. Inci, C. W. Park, S. Chung, N. R. Sottos, J. S. Moore, J. A. Rogers and S. R. White, *Adv. Mater.*, 2014, **26**, 7637–7642.

13 J. D. Wood, G. P. Doidge, E. A. Carrion, J. C. Koepke, J. A. Kaitz, I. Datye, A. Behnam, J. Hewaparakrama, B. Aruin, Y. Chen, H. Dong, R. T. Haasch, J. W. Lyding and E. Pop, *Nanotechnology*, 2015, **26**, 055302.

14 J. A. Kaitz, C. E. Diesendruck and J. S. Moore, *Macromolecules*, 2013, **46**, 8121–8128.

15 Cyclic PPA appears to be substantially more stable than end-capped, linear PPA (ref. 11).

16 A. M. DiLauro, G. S. Lewis and S. T. Phillips, *Angew. Chem. Int. Ed.,* 2015, DOI: 10.1002/anie.201501320R1.

17 This hypothesis was supported by substituent effect studies on the rate of hydrolysis of cyclic aromatic acetals: T. H. Fife, L. K. Jao, *J. Org. Chem.*, 1965, **30**, 1492–1495.

18 For example, the $pK_{a\,(DMSO)}$ value of a benzylic hydrogen in toluene is ~43–45, whereas the $pK_{a\,(DMSO)}$ value of a benzylic hydrogen in 4-nitrotoluene is 20.4: F. G. Bordwell, D. Algrims and N. R. Vanier, *J. Org. Chem.*, 1977, **42**, 1817–1819.

19 J. P. Guthrie, *J. Am. Chem. Soc.*, 2000, **122**, 5529–5538.

20 (a) O. Farooq, *Synthesis*, 1994, 1035–1036. (b) F. Garzino, A. Méou and P. Brun, *Helv. Chim. Acta*, 2002, **85**, 1989–1998. (c) G. Giorgi, F. J. Arroyo, P. López-Alvarado and J. C. Menéndez, *Tetrahedron*, 2011, **67**, 5582–5589. (d) Y. E. Türkmen, T. J. Montavon, S. A. Kozmin and V. H. Rawal, *J. Am. Chem. Soc.*, 2012, **134**, 9062–9065.

21 The THF-d_8 was used as received from the supplier. We used a new ampule for each experiment. The average water content (91 ± 4 ppm) for the THF-d_8 was calculated from data provided in the certificates of analysis for all ampules.

22 P. Ballinger, F. A. Long, *J. Am. Chem. Soc.*, 1960, **82**, 795–798.

23 Calculated using ACD/Labs Software, v11.02, Advanced Chemistry Development, Inc., Toronto, ON, Canada, 2015.

24 We used carbonic acid methyl ester for comparing pK_a values between carbonic acids and carboxylic acids. The $pK_{a\,(water)}$ for carbonic acid methyl ester is estimated to be 2.92 (ref. 25).

25 J. P. Guthrie, *Can. J. Chem.*, 1978, **56**, 2342–2354.

26 The pK_a value for benzoic acid in THF is 25.11: B. G. Cox, *Acids and Bases: Solvent Effects on Acid-Base Strength*, Oxford University Press, 2013.

27 (a) G. I. Peterson, M. B. Larsen and A. J. Boydston, *Macromolecules*, 2012, **45**, 7317–7328. (b) S. T. Phillips and A. M. DiLauro, *ACS Macro Lett.*, 2014, **3**, 298–304. (c) S. T. Phillips, J. S. Robbins, A. M. DiLauro, M. G. Olah, *J. Appl. Poly. Sci.*, 2014, **131**, 40992.

28 M. Frigerio, M. Santagostino and S. Sputore, *J. Org. Chem.*, 1999, **64**, 4537–4538.

29 A. R. Katritzky, Y.-J. Xu, A. V. Vakulenko, A. L. Wilcox and K. R. Bley, *J. Org. Chem.,* 2003, **68**, 9100–9104.

30 A. B. Pangborn, M. A. Giardello, R. H. Grubbs, R. K. Rosen and F. J. Timmers, *Organometallics*, 1996, **15**, 1518–1520.