On Demand Light-Degradable Polymers Based on 9,10-Dialkoxyanthracenes

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Light induced degradation of polymers has drawn increasing interest due to the need for externally controllable modulation of materials properties. However, the portfolio of polymers, that undergo precisely controllable degradation, is limited and typically requires UV light. A novel class of backbone-degradable polymers that undergo aerobic degradation in the presence of visible light, yet remain stable against broad-spectrum light under anaerobic conditions is reported. In this design, the polymer backbone is comprised of 9,10-dialkoxyanthracene units that are selectively cleaved by singlet oxygen in the presence of green light as confirmed by NMR and UV/vis spectroscopy. The resulting polymers have been processed by electrohydrodynamic (EHD) co-jetting into bicompartmental microfibers, where one hemisphere is selectively degraded on demand.

Backbone-degradable polymeric materials have attracted significant attention of polymer researchers due to their perspectives in drug delivery[1], biomaterials[2], nanocontainers,[3] and microreactors.[4] Backbone degradation can be achieved by different routes, for example, pH-controlled hydrolysis,[4,5] enzymatic degradation,[6] oxidation,[7] or light-induced reactions.[8] In many applications, light is a particularly compelling stimulus for degradation, because it acts as an external trigger that can be controlled with exceptional time and space resolution. Typically explored functional groups for light-induced degradation include ortho-nitrobenzyl esters,[9,10] truxillic acids (TRA),[11] and coumarins (CO),[12] among others. Unfortunately, polymers with these functional groups have their λ_{max} in the UV range (*o*NP ≈350 nm; TRA < 260 nm; CO ≈250 nm).[8] Extended exposure to UV light has been associated with phototoxicity in the past,[13] and among other factors, photocytotoxicity is one reason, why broader applicability of UV-degradable polymers has been limited.[14] In contrast, functional groups that can be cleaved by visible light are far less common[14,15] and, so far, have not yet been broadly explored in polymer chemistry[14–16] due to their very limited applications in our everyday life, where light is always present. Fundamentally, light-mediated degradation can be separated into light absorption and bond dissociation. In the past, DAs have been used in applications as a light cleavable linker for small molecules,[17] macromolecules,[16] and block copolymers,[14] in side chain modifications of polymers,[18,19] and as a sensor for singlet oxygen ($^1O_2$).[20,21]

Here, we report a new class of visible light-degradable polymers based on 9,10-dialkoxyanthracenes (DA, compound **1** in **Scheme 1**) that undergo aerobic degradation, but remain stable under anaerobic conditions, even in the presence of light. Decoupling the light absorption process from bond scission fundamentally enhances the level of control exhibited during polymer degradation.

To demonstrate cleavage of DAs, a photosensitizer, green light, and oxygen are required.[17] Eosin Y (**5**) as a photosensitizer was excited by green light (λ_{max} = 519 nm[22]) and transferred this energy to oxygen, generating singlet oxygen (Scheme 1). This then underwent a [2 + 4] cycloaddition reaction with the DA, forming an endo-peroxide (EPO) which was cleaved by catalytic amounts of protons.[23–25] Using this approach, the bond cleavage events are still orchestrated by the incoming light pulse, which is both, temporally and spatially controllable. Backbone cleavage occurred only when a photosensitizer and oxygen were concomitantly present. Since DAs as such do not bear functional groups which would allow a polymerization, we decided to use AA-type- and BB-type monomers for copper(I)-catalyzed azide alkyne cycloaddition (CuAAC) polymerization (**Scheme 2**).

This polymerization strategy allows for tuning the physico–chemical properties and solubilities of both, the final

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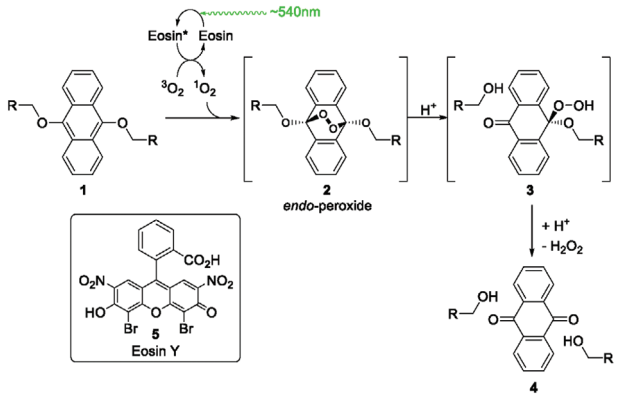
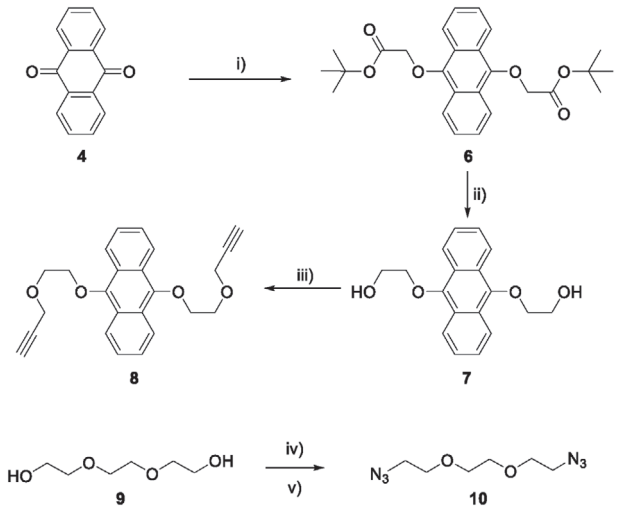
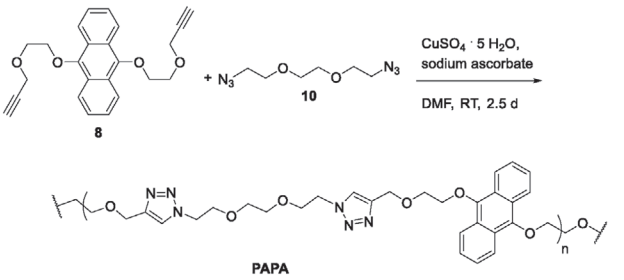


Scheme 1. Cleavage of 9,10-dialkoxyanthracenes (DA). Absorption of light is decoupled from the polymer backbone to Eosin. The hereby exited oxygen adds to the DA in a [2 + 4] fashion, converting it to the endo-peroxide **2** which is subsequently cleaved to yield 9,10-anthraquinone (**4**).

polymer and the degradation products by modification of the diazidomonomer and the dialkyne-DA. For example, instead of diadzidotriethyleneglyol (**10**), an aromatic or aliphatic diazidomonomer can easily be employed. There is a wide variety of natural products with an anthraquinone core, including drugs (anti-tumor, anti-inflammatory, anti-arthritic, anti-fungal, anti-bacterial, anti-malarial, antioxidant, and diuretic activities) and dyes,[26] hence employing a substituted DA, the degradation product could be a substituted AQ with designed secondary functions. Starting from triethyleneglycol (**9**), the diazidomonomer **10** was synthesized in two steps with an overall yield of 86%. The dialkyne-DA **8** was synthesized starting from 9,10-anthraquinone (**4**). Compound **4** was reduced to the corresponding dihydroxyanthracene, followed by in situ alkylation with *tert*-butyl bromoacetate, yielding the DA **6** in 83% yield. Subsequent ester reduction to the diol **7** with $LiAlH_4$ and alkylation with propargyl bromide yielded **8**. In this sequence, only **8**



Scheme 2. Synthesis of monomers. Conditions: i) $Na_2S_2O_4$, Adogen 464, NaOH, $tBuO_2CCH_2Br$, H_2O/DCM 1:1, 25°C, 24 h; 83%. ii) $LiAlH_4$, THF, 0 °C, 30 min; RT, 2 h; 83%. iii) Propargylbromid, NaH, THF, RT, 2 d; 58%. iv) TsCl, KOH, DCM, 0 °C, 3 h, quant. v) NaN_3, DMF, 80 °C, 24 h, 86%.



Scheme 3. CuAAC polymerization of **8** and **10** to PAPA (poly[(1,2-bis(2-azidoethoxy)ethane)-alt-(9,10-bis(2-(prop-2-yn-1-yloxy)ethoxy)anthracene)]).

was purified by column chromatography, whereas **6** and **7** only required a washing step with pentanes, making **8** accessible in three easy steps with a good overall yield of 40%.

After monomer synthesis, **8** and **10** were subjected to CuAAC polyaddition (**Scheme 3**). Employing copper sulphate and ascorbic acid as a catalyst system in DMF, poly[(1,2-bis(2-azidoethoxy)ethane)-alt-(9,10-bis(2-(prop-2-yn-1-yloxy)ethoxy)anthracene)] (PAPA) was obtained after 2.5 d at room temperature ($M_{n,NMR}$ = 14.8 kg × mol^{-1}, $M_{n,GPC}$ = 12.7 kg × mol^{-1}, $Đ_{m,GPC}$ = 1.74,[27] see ESI for full characterization). Prolonged reaction times led to solidification of the reaction mixture. The polymer was partly soluble, hindering GPC measurements for molecular weight determination.[28] With PAPA in hand, we next examined its on-demand degradation. A solution of PAPA and Eosin Y in DMSO-d_6 was illuminated with a 1 W green light LED in the presence of air.[29] Samples were withdrawn at different time points to monitor the reaction via ^{1}H-NMR.[30] To quantify the degradation under aerobic conditions, the integrals of the signals from the anthracene core from PAPA (δ = 7.47 and 8.30 ppm), the endo-peroxide (δ = 7.30 and 7.56 ppm) and of those from **4** (δ = 7.95 and 8.23 ppm) were determined. As expected, the signals from PAPA disappeared rapidly, when the solution was illuminated in the presence of air (**Figure 1**). After 70 min, the signals of the EPO still continued to grow before they ultimately disappeared. Concomitantly, the signals of **4** began to rise sharply after 35 min, indicating successful backbone cleavage. Full backbone cleavage was achieved within 3.5 h. In addition to the ^{1}H-NMR study, we also examined the reaction using UV/Vis analysis. UV/Vis traces were recorded at different time points during the cleavage experiment (**Figure 2**). The vanishing of anthracene signals around 400 nm was used as an indicator for backbone degradation of PAPA.[31]

In order to exclude other cleavage mechanisms, control experiments were carried out. Under anaerobic conditions or in the absence of Eosin Y, no backbone cleavage was observed (**Figure 3**). Without oxygen, 1% cleavage is observed after 24 h, most likely due to diffusion from oxygen through the septum of the reaction mixture. It is noteworthy, that with the use of Eosin Y disodium salt instead of Eosin Y, a delayed cleavage was observed. In the presence of 12 wt.% of Eosin Y disodium salt, polymer cleavage started 1.5 h after illumination and was completed within 2 h (see ESI Figure 1 for details).

Next, we intended to further elucidate the degradation process in the context of a more realistic biomaterial. To directly compare the degradation of PAPA relative to a hydrolytically degradable polyester, such as poly(lactide-co-glycolide) (PLGA),

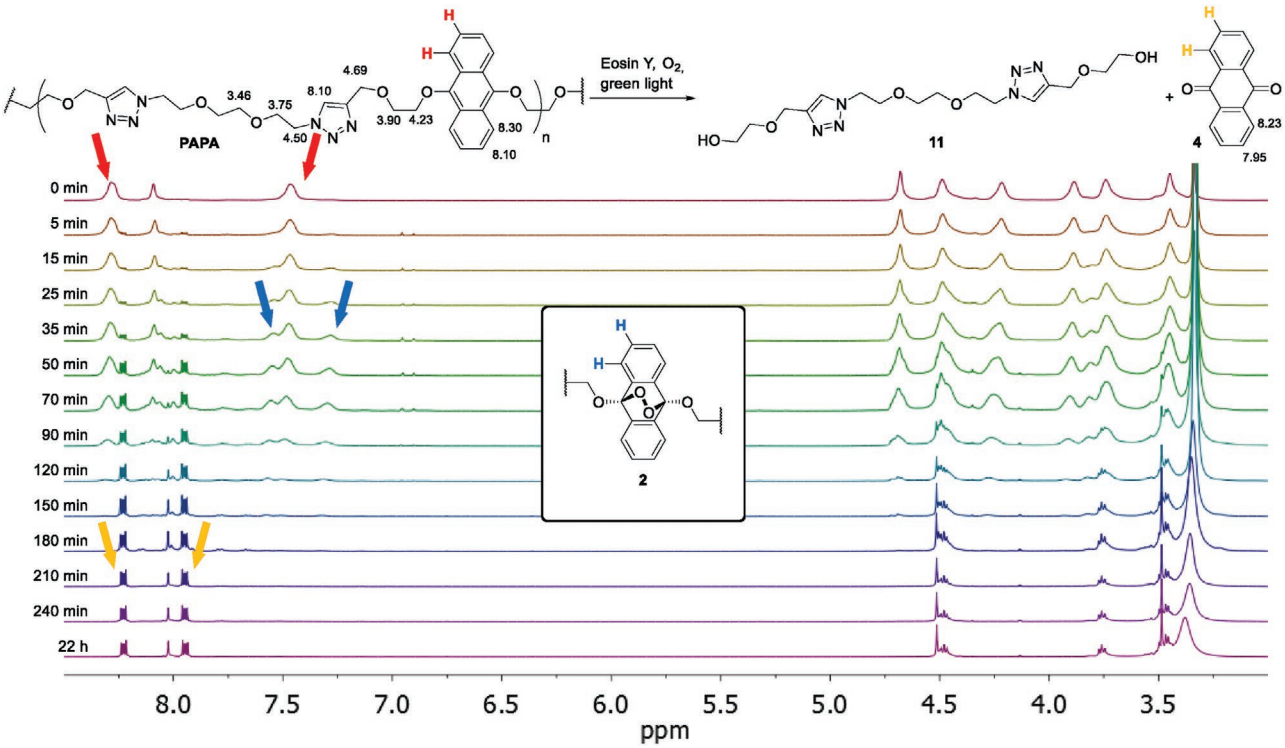


Figure 1. On-demand degradation of PAPA, numbers next to the carbon atoms in the equation are indicating the ^{1}H-NMR shifts for the corresponding protons, monitored by ^{1}H-NMR in DMSO-d_6. Signals of PAPA (δ = 7.47 and 8.30 ppm, marked in red), the endo-peroxide **2** (7.30 and 7.56 ppm, marked in blue) and **4** (7.95 and 8.23 ppm, marked in orange) were integrated to determine the ratio of polymer versus anthraquinone.

we created bicompartmental microfibers,[32] where one hemisphere contained PAPA as a major component and the second hemisphere was made entirely of PLGA. We prepared these anisotropic, bicompartmental microfibers by electrohydrodynamic (EHD) co-jetting. As this technique has been used to prepare multicompartmental microparticles,[33–38] fibers,[32,35,39] and complex 3D scaffolds,[40] successful processability would provide insights into the potential technological utility of PAPA.

For EHD co-jetting, polymer solutions were pumped through side-by-side[41] configured needles under a laminar flow. Applying high voltage between the needle and the collector generated a charge in the polymer solution, which accelerated the solution from the formed Taylor cone at the tip of the nozzle towards the collector. Hereby, the polymer solutions are stretched into a fine thread, leading to increased surface and therefore instantaneous drying. Generally, the polymer

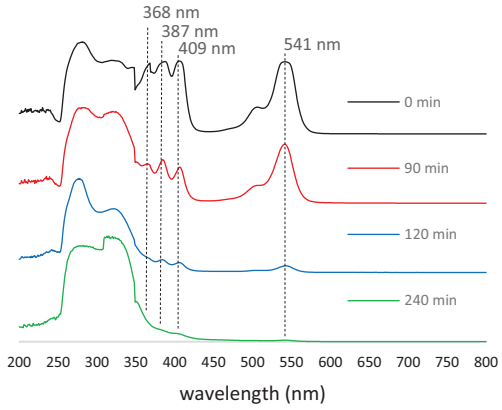


Figure 2. UV/Vis traces from selected time points during cleavage. The traces are shifted vertically for the sake of clarity. Signals at 368, 387, and 409 nm correspond to the anthracene core, signal at 541 nm corresponds to Eosin Y which is bleached due to excess $^1O_2$ after all PAPA is oxidized to the EPO.

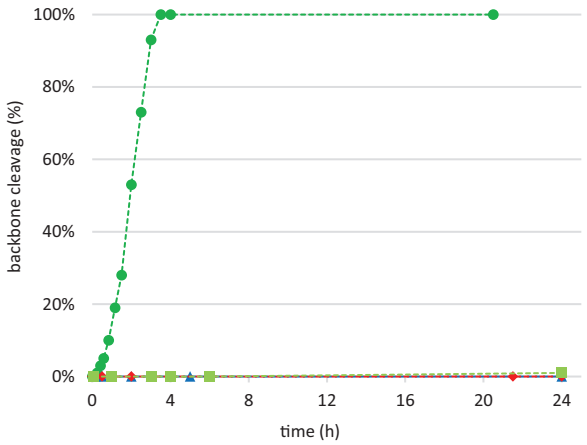


Figure 3. Backbone cleavage of PAPA in DMSO-d_6 over time (●, with 3 wt.% Eosin Y, constant bubbling with air, illumination with a 1 W green LED) and control experiments without light (■) oxygen (▲) or Eosin Y (◆).

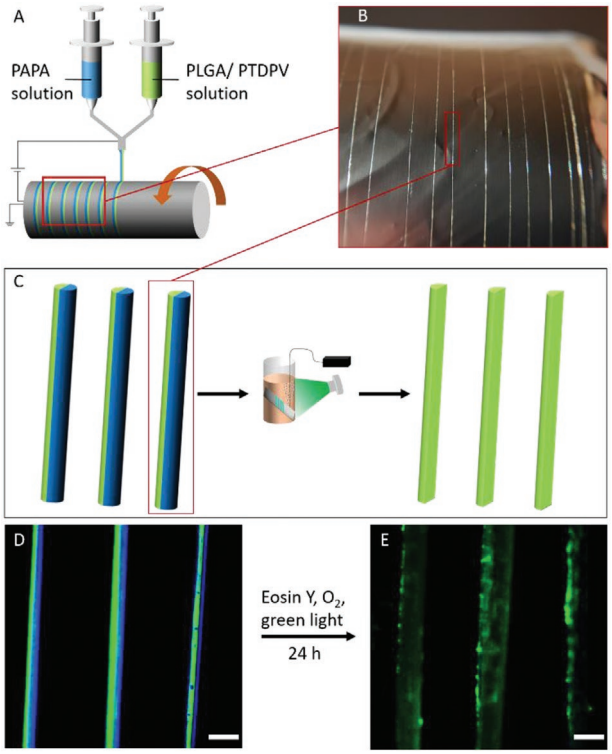


Figure 4. A) Schematic representation of EHD co-jetting on a rotating counter electrode. Indicated solvents were $CHCl_3$ / DMF, 97:3, for both solutions. B) Fibers jetted on the rotating counter electrode. C) Schematic representation of bicompartmental fibers (left), degradation setup (middle) and after degradation (right). D) PAPA-PLGA fibers imaged by CLSM. Blue: PAPA compartment, green: PLGA+PTDPV. For imaging the samples were transferred on a glass slide. E) Fibers after degradation for 24 h, imaged by CLSM with the same settings. All scale bars 50 µm.

thread can be collected as a continuous fiber or it can break up into particles, depending on the jetting conditions, which include, for example, flow rate, voltage, and concentration of the polymers.[34]

In order to obtain bicompartmental fibers, a ratio of 1:1 for degradable to non-degradable jetting solution was chosen. As polymer for the non-degradable compartment, PLGA (50–75 kDa) was chosen, as it is known for its good jetting properties. To realize the aspired fiber geometry, a side-by-side set up of two needles and a rotating counter electrode was used for EHD co-jetting (**Figure 4**A,B). By adding the dye poly[tris(2,5-bis(hexyloxy)-1,4-phenylenevinylene)-alt-(1,3-phenylenevinylene)] (PTDPV) to the PLGA compartment and using the inherent fluorescent properties of the DAs in PAPA, the fibers were imaged by confocal microscopy (Figure 4D,E). The bicompartmental microfibers with a diameter of 30 µm show two separate compartments, the PLGA compartment fluorescing green from PTDPV and the PAPA compartment fluorescing blue indicating the presence of anthracene groups.

Electrohydrodynamic co-jetting of PAPA and PLGA solutions using equal flow rates in a side-by-side set up resulted in microfibers in which PAPA was restricted to one hemispherical compartment (Figure 4D).

Next, the PAPA-PLGA microfibers were immersed into an aqueous Eosin Y solution (0.06 M) under illumination with green light and continuous bubbling with air to ensure oxygen saturation (Figure 4C). Not surprisingly, the heterogeneous degradation takes longer than in solution, which leads to a deformation of the PLGA compartment.

To confirm selective degradation of one hemispherical compartment, the microfibers were again imaged by CLSM, Figure 4E unambiguously confirms selective degradation of the PAPA polymer under aerobic conditions, whereas the PLGA compartment remained on the glass slide.

This communication establishes a new type of aerobically degradable, photoresponsive polymers, where the polymer backbone is rapidly degraded by visible light. This polymer is conveniently synthesized by CuAAC polyaddition from relatively inexpensive starting materials. Furthermore, bicompartmental microfibers, where one hemisphere can be selectively degraded on demand, have been demonstrated. This work thus opens new perspectives for the use of light degradable polymers as advanced materials, addressing some of the important drawbacks of current polymer systems,[8] such as the need for UV-light or the lack of precise temporal control.

Supporting Information

Supporting Information is available from the Wiley Online Library or from the author.

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Conflict of Interest

The authors declare no conflict of interest.

Keywords

backbone degradation, copolymers, singlet oxygen, sustainability, textiles

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