Supporting Information

A pH-triggered polymer degradation or drug delivery system by light-mediated cis / trans isomerization of o-hydroxy cinnamates

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1. Material and methods
Unless otherwise specified, all reagents, starting materials, and solvents (p.a. grade) were purchased from commercial suppliers (i.e. ABCR, Acros, Sigma-Aldrich, TCI, or Merck) and used as received without further purification. Synthesis of starting materials requiring oxygen- or moisture-sensitive reagents were carried out using flame-dried glassware, degassed solvents, and Schlenk lines. For the sake of clarity, $^1$H NMR data for all known compounds as well as a full characterization of new compounds are included in this section. Thin-layer chromatography (TLC) analyses were performed using pre-coated TLC-sheets ALUGRAM® Xtra SIL G/UV$_{254}$. Visualization was accomplished with UV light ($\lambda_{\text{max}} = 254$ nm). Column chromatography and flash chromatography were performed using silica gel with particle size 63 – 200 $\mu$m and 40 – 63 $\mu$m, respectively, as the stationary phase. UV/Vis measurements were performed on a Perkin Elmer LAMBDA 35. The molecular weight was estimated by size exclusion chromatography (GPC) using a liquid chromatograph (Shimadzu, model LC-8A, Tokyo, Japan) equipped with an Empower computer program (Waters, Milford, MA, USA). A PL HFIP gel column (Polymer Lab) and a refractive index detector (Shimadzu RID-10A, Tokyo, Japan) were employed. Buffers were adjusted by the pH meter HANNA HI 991001. High-resolution mass spectra (HRMS) were obtained according to the IUPAC recommendations (2013) from the central analytic mass spectrometry facilities of the Faculty of Chemistry and Pharmacy at the University of Regensburg. NMR spectra were recorded with a Bruker Avance 400 ($^1$H NMR: 400 MHz, $^{13}$C NMR: 101 MHz, $^{19}$F NMR: 376 MHz) or a Bruker Avance 300 ($^1$H NMR: 300 MHz, $^{13}$C NMR: 75 MHz, $^{19}$F NMR: 282 MHz).
Chemical shifts (δ) are reported in parts per million (ppm) relative to residual solvent peak (CHCl₃, 7.26 ppm). Coupling constants (J) are given Hertz (Hz). The following notations are used to indicate the multiplicity of the signals: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Photochemical reactions were performed using a custom-made set-up with an array of suitable LEDs (OSLON SSL 80, GD CS8PM1.14; 1 W, 3.5 V, 700 mA), i.e. λₑₓ = 455 ± 15 nm, connected to a power supply. The irradiation device was equipped with a stainless-steel jacket to maintain refrigeration of the vials. The distance between the LEDs and the reaction vials was adjusted to 0.9 ± 0.1 cm. The apparatus also allows the magnetic stirring of the reaction mixtures. The reported yields are referred to as the isolated compounds unless otherwise stated. Oxygen- and moisture-free reactions were carried out with dry and degassed solvents, as well as glassware subjected to several evacuations (vacuum)/refill (nitrogen) cycles.

Poly(ethylene glycol) based compounds like poly(ethylene glycol) bis(azide); Mᵣⁿ=200¹, poly(ethylene glycol) bis(azide); Mᵣⁿ=2000² and poly(ethylene glycol) methyl ether azide; Mᵣⁿ=2000² were synthesized according to the corresponding literature procedures.

2. Synthesis

2.1. Synthesis of cinnamates

*General procedure A:*

![Cinnamate reaction scheme](image)

The cinnamate derivatives 1 were synthesized according to the literature³ with minor differences: To a solution of the *ortho*-hydroxy benzaldehyde derivative (1 equiv) in dry CH₂Cl₂ (45 equiv) was added triphenyl-λ⁵-phosphanylidene derivative (1.3 equiv) and the mixture was refluxed and monitored by TLC. Afterward the solvent was evaporated under
reduced pressure and the residue was purified by chromatography using a mixture of hexanes
and ethyl acetate as eluent giving the desired compounds 1. Spectroscopical data matched the
literature.\textsuperscript{[3]}

2.2. Synthesis of coumarins

General procedure B:

In an 8 mL vial equipped with a magnetic stir bar 2-hydroxy cinnamates 1 (0.25 mmol) and
20 mol\% DIPEA in acetonitrile (1 mL) were added. The vial was closed with a septum and
subjected to three freeze-pump-thaw cycles for degassing and subsequently irradiated with a
LED ($\lambda_{\text{Ex}} = 455$ nm) for 4 h. Evaporation of the solvent and purification on silica
(hexanes/EtOAc) gave the desired compounds 2.

\textit{Coumarin 2a}

The NMR data was matching the literature\textsuperscript{[4]}:

Synthesized according to general procedure A (33.6 mg, 0.230 mmol, 92 %).

R\textsubscript{f} 0.18 (hexanes/EtOAc 9:1); \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) $\delta$ 7.65 (d, $J = 9.6$ Hz, 1H), 7.40 (d, $J = 7.5$ Hz, 2H), 7.23 – 7.10 (m, 2H), 6.27 (d, $J = 9.6$ Hz, 1H).

\textit{7-Hydroxycoumarin 2b}

The NMR data was matching the literature\textsuperscript{[5]}:

Synthesized according to general procedure A (37.7 mg, 0.232 mmol, 93 %).

R\textsubscript{f} 0.15 (hexanes/EtOAc 7:3); \textsuperscript{1}H NMR (300 MHz, DMSO) $\delta$ 10.59 (s, 1H), 7.93 (d, $J = 9.5$ Hz, 1H), 7.52 (d, $J = 8.2$ Hz, 1H), 6.78 (dd, $J = 8.3$, 2.6 Hz, 1H), 6.72 (t, $J = 4.5$ Hz, 1H), 6.20 (d, $J = 9.4$ Hz, 1H).
3-Methylcoumarin 2c
The NMR data was matching the literature\cite{6}:

Synthesized according to general procedure A (38.4 mg, 0.240 mmol, 96%).

R_f 0.30 (hexanes/EtOAc 9:1); \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \textbf{δ} 7.52 (s, 1H), 7.49 – 7.39 (m, 2H), 7.31 (d, J = 8.2 Hz, 1H), 7.28 – 7.21 (m, 1H), 2.21 (d, J = 1.3 Hz, 3H).

3-Methyl-7-hydroxycoumarin 2d
The NMR data was matching the literature\cite{7}:

Synthesized according to general procedure A (43.6 mg, 0.248 mmol, 99%).

R_f 0.23 (hexanes/EtOAc 7:3); \textsuperscript{1}H NMR (300 MHz, DMSO) \textbf{δ} 10.39 (s, 1H), 7.42 (d, J = 8.4 Hz, 1H), 6.76 (dd, J = 8.4, 2.3 Hz, 1H), 6.69 (d, J = 2.3 Hz, 1H), 2.03 (s, 3H).

4-Methylcoumarin 2e
The NMR data was matching the literature\cite{4}:

Synthesized according to general procedure A (32.0 mg, 0.200 mmol, 80%).

R_f 0.18 (hexanes/EtOAc 9:1); \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}) \textbf{δ} 7.59 (d, J = 7.7 Hz, 1H), 7.52 (t, J = 7.7 Hz, 1H), 7.34 – 7.24 (m, 2H), 6.28 (s, 1H), 2.43 (s, 3H).

3-Allylcoumarin 2f
The NMR data were matching the literature\cite{8}:

Synthesized according to general procedure A (45.6 mg, 0.245 mmol, 98%).

R_f 0.30 (hexanes/EtOAc 9:1); \textsuperscript{1}H NMR (300 MHz, DMSO) \textbf{δ} 7.82 (q, J = 1.0 Hz, 1H), 7.67 (dd, J = 7.7, 1.6 Hz, 1H), 7.56 (ddd, J = 8.7, 7.3, 1.6 Hz, 1H), 7.38 (d, J = 8.4 Hz, 1H), 7.33 (td, J = 7.5, 1.2 Hz, 1H), 5.97 (ddt, J = 16.8, 10.0, 6.6 Hz, 1H), 5.25 – 5.10 (m, 2H), 3.23 (dq, J = 6.6, 1.4 Hz, 2H); \textsuperscript{13}C NMR (75 MHz, DMSO) \textbf{δ} 161.04, 153.06, 139.84, 134.85, 131.48, 128.34, 127.49, 124.94, 119.65, 118.07, 116.38, 34.51.
7-(Propargyloxy)-coumarin 2g
The NMR data was matching the literature[9]:

Synthesized according to general procedure A (49.0 mg, 0.245 mmol, 98%).

Rf 0.25 (hexanes/EtOAc 7:3); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.65 (d, $J = 9.5$ Hz, 1H), 7.40 (d, $J = 8.5$ Hz, 1H), 6.95 (d, $J = 2.4$ Hz, 1H), 6.91 (dd, $J = 8.5$, 2.5 Hz, 1H), 6.29 (d, $J = 9.5$ Hz, 1H), 4.77 (d, $J = 2.4$ Hz, 2H), 2.58 (t, $J = 2.4$ Hz, 1H); GC-MS (EI) m/z: [M]$^{+*}$ calcd for C$_{12}$H$_8$O$_3$, 200.05; found 200.0473.

2.3. Synthesis of oHC-bis(Alk) 1g

Scheme S1. Synthesis overview of the monomer 1g; Reaction conditions a) propargyl alcohol pyridine, CH$_2$Cl$_2$, 0 to r.t., 1 h. b) 1) PPh$_3$, C$_7$H$_8$, r.t. 16 h 2) NaOH (2M), 30 min. c) K$_2$CO$_3$, propargyl bromide, acetone, reflux, 3 h. d) CH$_2$Cl$_2$, reflux, 2 h.

Propargyl bromoacetate S1
The compound was synthesized according to the literature procedure[10] with minor differences:

Bromoacetyl bromide (2.61 mL, 30.0 mmol, 1 equiv) was added dropwise to a solution of propargyl alcohol (1.73 mL, 30 mmol, 1 equiv) and pyridine (2.4 mL, 30 mmol, 1 equiv) in CH$_2$Cl$_2$ (40 mL) at 0 °C to form a white suspension that was stirred for 20 min at 0 °C and then an additional 30 min at 25 °C. At this time, H$_2$O (50 mL) was added to the reaction mixture and the organic layer was separated. The aqueous layer was then extracted with CH$_2$Cl$_2$ (2 mL x 20). The combined organic layers were washed with brine (50 mL) and dried over Na$_2$SO$_4$. The filtrate was then concentrated to give S1 as a colorless liquid which was used directly without purification for the next step.
Propargyl-(triphenyl-λ5-phosphaneylidene)acetate S2
The compound was synthesized according to the literature procedure[10] with minor differences:

Propargyl bromoacetate was added dropwise to a toluene solution (100 mL) of triphenylphosphine (7.8 g, 30 mmol, 1 equiv) to form a white precipitate. The resulting slurry was stirred overnight, filtered over a glass fritted filter, and washed with toluene and hexanes to give phosphonium salt as a white solid. The white solid was dissolved in H₂O (100 mL) and NaOH (2 M) was added to keep the aqueous pH > 7. A white solid appeared, and the mixture was stirred for 30 min before CH₂Cl₂ (50 mL) was added. The organic layer was separated and washed with brine (50 mL) and dried over Na₂SO₄. The filtrate was concentrated to give phosphorane S2 as a white solid which was used directly without further purification for the next step.

2-Hydroxy-4-prop-2-ynyloxy-benzaldehyde S3
The compound was synthesized according to the literature procedure[11] with minor differences:

A flask was charged with dry acetone (50 ml), 2,4-dihydroxybenzaldehyde (5 g, 36 mmol, 1 equiv) and potassium carbonate (5 g, 36 mmol, 1 equiv). The mixture was heated to 50 °C, to this reaction mixture, propargyl bromide solution (3.4 ml, 36 mmol, 1 equiv; 80 wt. % solution in toluene) was slowly added via syringe. Then, the reaction mixture was stirred for 3 h under reflux. After cooling to room temperature, the mixture was concentrated under vacuum and DCM (180 ml) was added. The organic layer was washed four times with water, dried over Na₂SO₄, filtered and concentrated. Purification by silica gel chromatography (hexanes/CHCl₃ 1:1) afforded the desired product S3 as a white solid (1.90 g, 10.8 mmol, 30 %).

The NMR data was matching the literature[11]:

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Propargyl-3-(2-hydroxy-4-(propargyloxy)phenyl)acrylate \textit{1g}

The compound was synthesized according to the literature procedure\textsuperscript{[3]} with minor differences:

To a solution of 2-hydroxy-4-prop-2-ynyloxy-benzaldehyde (500 mg, 2.84 mmol, 1 equiv) in dry CH\textsubscript{2}Cl\textsubscript{2} (8 mL) was added propargyl-(triphenyl-\lambda\textsuperscript{5}-phosphaneylidene)acetate (1.35 g, 3.7 mmol, 1.3 equiv) and the mixture was refluxed for 2 h. After the reaction completed (monitored by TLC), the solvent was evaporated under reduced pressure. The residue was purified by silica gel chromatography (hexanes/10 - 30 % EtOAc) eluting the desired compound \textit{1g} as white crystals (630 mg, 2.3 mmol, 86 %).

R\textsubscript{f} 0.19 (hexanes/EtOAc 4:1); \textit{\textsuperscript{1}H} NMR (300 MHz, DMSO) \(\delta\) 10.49 (s, 1H), 7.84 (d, \(J = 16.1\) Hz, 1H), 7.60 (d, \(J = 8.4 \) Hz, 1H), 6.57 – 6.46 (t, 2H), 6.50 (d, \(J = 13.2\) Hz, 1H), 4.79 (d, \(J = 2.4 \) Hz, 4H), 3.63 (t, \(J = 2.4\) Hz, 1H), 3.56 (t, \(J = 2.4\) Hz, 1H); \textit{\textsuperscript{13}C} NMR (75 MHz, DMSO) \(\delta\) 166.62, 160.79, 158.85, 141.34, 130.89, 114.91, 114.05, 107.21, 102.53, 79.39, 79.26, 79.07, 77.98, 55.93, 51.88; IR(neat): 3284, 3247, 2361, 1672, 1601, 1512, 1434 cm\textsuperscript{-1}; HRMS (ESI) \textit{m/z}: [M-H]\textsuperscript{-} calcd for C\textsubscript{15}H\textsubscript{12}O\textsubscript{4}, 255.07; found 255.0676. Anal. calcd for C\textsubscript{15}H\textsubscript{12}O\textsubscript{4}: C 70.31, H 4.72, O 24.97; found: C 70.68, H 4.81, O 24.51; Mp.: 122 °C.

\textbf{2.4. Synthesis of the polymer 3a/3b}
Scheme S2. Synthesis overview of 3a/3b via CuAAC "click" reaction; Reaction conditions: 1g, PEGₙ-bis(azide), Cu(I)I, DMF, 70 °C, 16 h.

**Poly(PEG₂₀₀-alt-oHC) 3a**

In a septum sealed vial propargyl-3-(2-hydroxy-4-(propargyloxy)phenyl)acrylate (75 mg, 0.3 mmol, 1 equiv), the corresponding PEG-bis(azide) (0.3 mmol, 1 equiv) and Cu(I)I (6 mg, 0.03 mmol, 0.1 equiv) was dissolved in DMF (1.5 mL) and subjected to ultrasonication for 1 min. The vial was sealed, N₂ was bubbled through the solution for 15 min and the polymerization was carried out in an aluminum heating block for 16 h at 70 °C. Afterward, the solvent was removed in vacuo and the resulting polymer 3a (145 mg) was used without further purification.

¹H NMR (300 MHz, DMSO) δ 10.42 (s, 1H), 8.16 (d, J = 12.0 Hz, 2H), 7.81 (d, J = 16.0 Hz, 1H), 7.53 (d, J = 8.8 Hz, 1H), 6.57 – 6.41 (m, 3H), 5.22 (s, 2H), 5.12 (s, 2H), 4.51 (t, J = 5.2 Hz, 4H), 3.78 (t, J = 5.2 Hz, 4H), 3.53 – 3.32 (m, 8H).

**Poly(PEG₂₀₀₀-alt-oHC) 3b**

In a septum sealed vial propargyl-3-(2-hydroxy-4-(propargyloxy)phenyl)acrylate (75 mg, 0.3 mmol, 1 equiv), the corresponding PEG-bis(azide) (0.3 mmol, 1 equiv) and Cu(I)I (6 mg, 0.03 mmol, 0.1 equiv) was dissolved in DMF (1.5 mL) and subjected to ultrasonication for 1 min. The vial was sealed, N₂ was bubbled through the solution for 15 min and the polymerization was carried out in an aluminum heating block for 16 h at 70 °C. Afterward, the polymer mixture was precipitated in 100 mL Et₂O, decanted, dissolved in the least amount of DCM (~1-2 mL) and precipitated in 100 mL Et₂O. This purification method was repeated five times to remove the DMF, then the material was dried in vacuo for 48 h yielding the resulting polymer 3b (523 mg).
$^1$H NMR (300 MHz, DMSO) δ 10.42 (s, 1H), 8.17 (d, $J = 11.5$ Hz, 2H), 7.81 (d, $J = 16.1$ Hz, 1H), 7.55 (d, $J = 9.2$ Hz, 1H), 6.55 (d, $J = 6.9$ Hz, 2H), 6.48 (d, $J = 16.1$ Hz, 1H), 5.22 (s, 2H), 5.12 (s, 2H), 4.54 (t, $J = 5.0$ Hz, 4H), 3.82 (t, $J = 5.3$ Hz, 4H), 3.50 (s, 192H). IR(neat): 2878, 1709, 1609, 1467, 1344, 1281, 1244, 1147, 1100, 1061 cm$^{-1}$. 
2.5. Synthesis of mPEG\textsubscript{2000}-oHC-drug 5a/5b

\begin{figure}
\centering
\includegraphics[width=\textwidth]{scheme.png}
\caption{Scheme S3. Synthesis overview of 5a/5b; Reaction conditions a) DCC, DMAP, CH\textsubscript{2}Cl\textsubscript{2}, r.t., 16 h. b) PPh\textsubscript{3}, NaOH/H\textsubscript{2}O, toluene, r.t., 16 h. c) mPEG\textsubscript{2000}-N\textsubscript{3}, Cu(J)l, DMF, 65 °C, 18 h. d) CH\textsubscript{2}Cl\textsubscript{2}, reflux, 2 h.}
\end{figure}

2-(Triphenyl phosphaneylidene)acetates S5a/S5b

The compounds were synthesized according to the literature procedure\textsuperscript{[12]} with minor differences:

2-Bromoacetic acid (6 mmol, 1.2 equiv) and the corresponding alcohol (5 mmol, 1.0 equiv) were dissolved in CH\textsubscript{2}Cl\textsubscript{2} (40 mL) in a 100 mL round-bottom flask with a stir bar, then DCC (6 mmol, 1.2 equiv) was added to the mixture, followed by adding a catalytic amount of DMAP (0.5 mmol, 0.1 equiv), the mixture was stirred overnight at room temperature. Afterward the mixture was filtered, extracted with brine (3 x 30 mL), dried with Na\textsubscript{2}SO\textsubscript{4}, and subjected to silica gel column chromatography (hexanes/EtOAc 19:1) to afford the desired bromoacetates S4a/S4b.

In a 100 mL round-bottom flask equipped with a magnetic stir bar, triphenylphosphine (4.06 mmol, 1 equiv) was dissolved in toluene (30 mL) and bromoacetate (4.06 mmol, 1 equiv) was added to this solution slowly. The solution was stirred at room temperature and a white precipitate formed. The reaction was monitored by TLC (hexanes/EtOAc 20:1). After
complete consumption of starting material, the precipitate was filtered and washed with EtOAc and dried to afford the phosphonium salt.

The obtained phosphonium salt was dissolved in DCM (30 mL) and H₂O (15 mL) was added. To the stirred two-phase system, NaOH solution (4.06 mmol, 1 equiv) was added until the pH reached stable basic conditions. Afterward, the organic phase was separated, and the water phase was extracted with DCM (2 x 30 mL). The combined organic layers were washed with brine (1 x 30 mL), dried over Na₂SO₄, filtered, and dried in vacuo to afford the desired ylide S₅a/S₅b as a white solid powder. The compound was used without further purification.

**mPEG₂₀₀₀°-OH-benzaldehyde S₆**

In a septum sealed vial mPEG₂₀₀₀-N₃ (0.5 g, 0.24 mmol, 1 equiv), 2-hydroxy-4-prop-2-ynyloxy-benzaldehyde (51 mg, 0.29 mmol, 1.2 equiv) and Cu(I)I (5 mg, 0.024 mmol, 0.1 equiv) were dissolved in DMF (2 mL) and degassed by bubbling with a stream of N₂ through the solution. The reaction vessel was stirred in a preheated aluminum block at 65 °C for 18 h. After that the Cu(I)I salt was centrifuged and the solution was precipitated into cold Et₂O (5 x 100 mL) from the least amount of DCM (~1-2 mL) to remove all DMF residues. The product S₆ was dried under vacuo and used without further purification.

¹H NMR (300 MHz, CDCl₃) δ 11.43 (s, 1H), 9.72 (s, 1H), 7.89 (s, 1H), 7.44 (d, J = 8.6 Hz, 1H), 6.63 (dd, J = 8.7, 2.4 Hz, 1H), 6.54 (d, J = 2.3 Hz, 1H), 5.24 (s, 2H), 4.56 (t, J = 4.9 Hz, 1H), 3.79 – 3.54 (m, 248H), 3.36 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 194.50, 165.37, 164.29, 135.41, 115.47, 108.57, 101.76, 71.90, 70.54, 70.42, 69.31, 62.22, 59.02, 50.42; IR(neat): 2882, 1635, 1471, 1344, 1285, 1244, 1147, 1110, 1061 cm⁻¹; Anal. calcd for C₁₅H₁₂O₄: C 57.54, H 8.43, N 1.77, O 32.27; found: C 55.51, H 8.37, N 1.36, O 34.76; Mp.: 50 °C.
mPEG_{2000-oHC-drug} 5a/5b
In a 25 mL Schlenk flask mPEG_{2000-o-OH-benzaldehyde} (0.074 mmol, 1 equiv) and the corresponding phosphonium ylide (0.088 mmol, 1.2 equiv) were dissolved in dry DCM (6 mL) under a stream of N₂ and the solution was refluxed for 16 h. Afterward the solvent was reduced to the least amount (~1-2 mL) and precipitated into cold Et₂O (100 mL), centrifuged, decanted and re-dissolved in the least amount of DCM (~1-2 mL). This procedure was repeated for five times. The material was dissolved in H₂O (1 mL), centrifuged and the supernatant was lyophilized for 24 h. The pure mPEG_{2000-oHC-drug} was obtained as a slightly yellow solid material 5a (120 mg, 0.052 mmol, 45 %); 5b (108 mg, 0.045 mmol, 62 %).

5a: ¹H NMR (300 MHz, DMSO) δ 10.56 (s, 1H), 8.23 (d, J = 11.8 Hz, 1H), 7.97 (d, J = 16.1 Hz, 1H), 7.79 – 7.72 (m, 3H), 7.65 (d, J = 9.9 Hz, 1H), 7.44 (t, J = 7.9 Hz, 1H), 7.27 (t, J = 7.4 Hz, 1H), 7.18 (d, J = 7.4 Hz, 1H), 6.71 (d, J = 16.1 Hz, 1H), 6.64 – 6.56 (m, 1H), 5.21 (d, J = 34.0 Hz, 2H), 4.55 (t, J = 5.1 Hz, 2H), 3.83 (t, J = 4.7 Hz, 2H), 3.79 – 3.37 (m, 219H), 3.24 (s, 3H); IR(neat): 2882, 1720, 1605, 1471, 1344, 1281, 1240, 1195, 1151, 1110, 1061 cm⁻¹; Anal. calcd for C_{107}H_{193}N_{3}O_{48}: C 56.13, H 8.5, N 1.84, O 33.54; found: C 55.89, H 8.37, N 1.49, O 34.25; Mp.: 48 °C.

5b: ¹H NMR (300 MHz, DMSO) δ 10.56 (s, 1H), 8.23 (d, J = 13.6 Hz, 1H), 7.97 (d, J = 16.5 Hz, 1H), 7.92 – 7.83 (m, 1H), 7.80 – 7.72 (m, 2H), 7.70 – 7.51 (m, 5H), 7.44 (t, J = 7.8 Hz, 2H), 7.27 (t, J = 7.3 Hz, 1H), 7.18 (d, J = 7.4 Hz, 2H), 6.71 (d, J = 16.2 Hz, 1H), 6.57 (s, 1H), 5.21 (d, J = 34.6 Hz, 2H), 4.55 (t, J = 5.1 Hz, 2H), 3.82 (t, J = 5.2 Hz, 2H), 3.77 – 3.38 (m, 229H), 3.24 (s, 3H); IR(neat): 2882, 1709, 1609, 1471, 1344, 1281, 1240, 1195, 1151, 1110, 1061 cm⁻¹; Anal. calcd for C_{114}H_{199}N_{3}O_{48}: C 57.54, H 8.43, N 1.77, O 32.27; found: C 56.01, H 8.40, N 1.46, O 34.14; Mp.: 47 °C.
3.1. Characterization of 3a/3b by $^1$H NMR

The final polymer 3a was characterized by NMR analysis. The synthesis of the polymer was confirmed by the triazole peaks at 8.18 and 8.14 ppm (b) (see Figure S1, B) and the incorporation of the PEG$_{200}$-bis(azide) monomer at 3.30-3.51 ppm, 3.78 and 4.51 ppm (j, i and h, respectively) and the oHC-bis(alkyne) moiety at 6.50, 7.53, and 7.81 ppm (e, f, d and c) as well as the phenolic proton at 10.42 ppm (a). The CH$_2$-junctions at the triazole rings can be found grouped at 5.12 and 5.22 ppm ($g_1$ and $g_2$) (see Figure S1, B).

Figure S1. A) Representative $^1$H NMR of the cleaving product obtained after irradiation of 3a in DMF, measured in DMSO-$d_6$. B) Representative $^1$H NMR of the polymer material 3a measured in DMSO-$d_6$. 
3.2. Photocleavage experiments

![Figure S2](image_url) 1.5 mM solutions of 3b in 0.1M Britton-Robinson buffer (left) pH=2.1, (mid) pH=7.4 and (right) pH=11.8.

*Photocleavage of 1g monitored by $^1$H NMR*

In a septum-sealed vial equipped with a magnetic stirrer, a 0.25 mM solution of 1g in dry MeCN was degassed by bubbling with a stream of N$_2$ for 15 min. Afterward 20 mol% DIPEA was added by syringe through the septum and the vessel was irradiated ($\lambda_{Ex} = 455$ nm) for 2 h under stirring, while 20 µL samples were taken in a 10 min interval for 60 min and one last sample at 120 min. The collected samples were dried under vacuum for 48 h, dissolved in 0.6 mL of CDCl$_3$ and subjected to $^1$H NMR spectroscopy. The doublet from the (CH$_2$)-allylene group at 4.81 ppm was monitored in comparison to the doublet-peak from the newly formed (CH$_2$)-allylene of the aryl ether at 4.77 ppm, which shifted downfield during this process from 4.67 ppm (see Figure S3).
Figure S3. Time-dependent photocleavage of $1g$ followed by $^1$H NMR spectroscopy in CDCl$_3$. 
Photocleavage of 3a to 4a monitored by $^1$H NMR

In a septum-sealed vial equipped with a magnetic stirrer 50 mg of 3a in dry DMF (1 mL) was degassed by bubbling with a stream of N$_2$ for 15 min. Afterward, DIPEA (40 µL) was added by syringe through the septum and the vessel was irradiated ($\lambda_{\text{Ex}} = 455$ nm) for 2 h, while 20 µL samples were taken in a 10 min interval for 60 min and one last sample at 120 min, if necessary. The collected samples were dried under vacuum for 48 h, dissolved in 0.6 mL of deuterated DMSO and subjected to $^1$H NMR spectroscopy. The shift of $g_1$ and $g_2$ peaks (Figure S1 and Figure S4) was monitored over time.

$^1$H NMR of the corresponding degradation product 4a after irradiation: $^1$H NMR (300 MHz, DMSO) $\delta$ 8.23 (d, $J = 3.3$ Hz, 1H), 7.99 (dd, $J = 9.5, 4.1$ Hz, 1H), 7.92 (s, 1H), 7.63 (dd, $J = 8.7, 4.4$ Hz, 1H), 7.16 (dd, $J = 5.1, 2.4$ Hz, 1H), 7.01 (ddd, $J = 8.6, 4.7, 2.4$ Hz, 1H), 6.30 (dd, $J = 9.5, 3.0$ Hz, 1H), 5.25 (d, $J = 3.4$ Hz, 2H), 5.17 (d, $J = 6.2$ Hz, 1H), 4.51 (dq, $J = 15.7, 5.0$ Hz, 5H), 3.79 (p, $J = 5.3$ Hz, 4H), 3.53 – 3.39 (m, 8H).

![Figure S4](image)

**Figure S4.** Time-dependent photocleavage of 3a to 4a followed by H NMR spectroscopy measured in CDCl$_3$. 
**Figure S5.** Photocleavage of 1g and 3a with 20 mol% DIPEA in MeCN followed by $^1\text{H}$ NMR spectroscopy in CDCl$_3$ and DMSO-$d_6$, respectively.

**Photocleavage of 3b to 4b monitored by $^1\text{H}$ NMR**

In a septum-sealed vial equipped with a magnetic stirrer 3b (100 mg) in a suitable buffer (2 mL) was degassed by bubbling with a stream of N$_2$ for 15 min. Afterward, the vessel was irradiated ($\lambda_{\text{Ex}} = 455 \text{ nm}$) for 2 h, while 0.2 mL samples were collected into Eppendorf cups during a given time interval. The collected samples were freeze-dried until complete removal of water, dissolved in 0.6 mL of CDCl$_3$ and the soluble part was subjected to $^1\text{H}$ NMR spectroscopy. The shift of $g_1$ and $g_2$ peaks (**Figure S1** and **Figure S6**) was monitored over time.

$^1\text{H}$ NMR of the corresponding degradation product 4b after irradiation: $^1\text{H}$ NMR (300 MHz, CDCl$_3$) $\delta$ 7.91 (s, 1H), 7.83 (s, 1H), 7.64 (d, $J = 9.5 \text{ Hz}$, 1H), 7.39 (d, $J = 9.2 \text{ Hz}$, 1H), 7.00 – 6.85 (m, 2H), 6.26 (d, $J = 9.5 \text{ Hz}$, 1H), 5.26 (s, 2H), 4.78 (s, 2H), 4.56 (dt, $J = 8.1$, 5.0 Hz, 4H), 3.94 – 3.81 (m, 4H), 3.77 – 3.45 (m, 186H).
Figure S1. Time dependent photodegradation of 3b to 4b followed by H NMR in (top, left) 0.1M HCl/KCl buffer (pH=2.1) (top, right) 0.01 M PBS buffer (pH = 5.5), (center, left) 0.01 M PBS buffer (pH = 6.5), (center, right) 0.01 M PBS buffer (pH = 7.4) and (bottom, left) 0.1 M carbonate buffer (pH = 9.2) measured in CDCl$_3$. (Bottom, right) 0.01 M PBS buffer (pH = 6.5) integration of $g_1/g_2$ at 0 min and 120 min.

**Photocleavage of 3b to 4b monitored by UV/Vis spectroscopy**

In a septum-sealed vial equipped with a magnetic stirrer 100 mg of 3b in 2 mL 0.1M Britton-Robinson buffer (pH = 6.50) was degassed by bubbling with a stream of N$_2$ for 15 min.
Afterward, the vessel was irradiated ($\lambda_{\text{Ex}} = 455 \text{ nm}$) for 2 h, while 0.20 mL samples were taken in a 10 min interval for 60 min and one last sample at 120 min and filled up to 1 mL with 0.1M Britton-Robinson buffer (pH = 11.8) and used as stock solutions. The samples were diluted with 0.1M Britton-Robinson buffer (pH = 11.8) to 62 $\mu$M and measured.

**Photocleavage of 3b to 4b monitored by fluorescence spectroscopy**

In a septum-sealed vial equipped with a magnetic stirrer 100 mg of 3b in 2 mL 0.1M Britton-Robinson buffer (pH = 6.5) was degassed by bubbling with a stream of N$_2$ for 15 min. Afterward, the vessel was irradiated ($\lambda_{\text{Ex}} = 455 \text{ nm}$) for 2 h, while 0.20 mL samples were taken in a 10 min interval for 60 min and one last sample at 120 min and filled up to 1 mL with 0.1M Britton-Robinson buffer (pH = 11.8) and used as stock solutions. The samples were diluted with 0.1M Britton-Robinson buffer (pH = 11.8) to 1.55 nM and measured.

![Figure S7](image-url)  
**Figure S7.** A) Time-dependent photocleavage process of 3b in 0.01M PBS buffer (pH 6.5) monitored by UV/Vis spectroscopy. B) Time-dependent photocleavage process of 3b in 0.01M PBS buffer (pH 6.5) monitored by fluorescence spectroscopy exciting at 410 nm.

**Photocleavage of 3b to 4b monitored by GPC**

In a septum-sealed vial equipped with a magnetic stirrer 100 mg of 3b in 2 mL 0.1M Britton-Robinson buffer (pH = 6.50) was degassed by bubbling with a stream of N$_2$ for 15 min. Afterward, the vessel was irradiated ($\lambda_{\text{Ex}} = 455 \text{ nm}$) for 2 h, while 0.20 mL samples were taken in a 10 min interval for 60 min and one last sample at 120 min. The samples were
freeze-dried until complete removal of water. The polymer was dissolved and eluted in 1,1,1,3,3,3-hexafluoropropanol (HFIP) containing CF₃COONa (0.05 M) at a flow rate of 1 mL/min (injected volume 20 μL, sample concentration 15.0 mg/mL). The number and weight average molecular weights were calculated using polymethyl methacrylate standards.
**Determination of $pK_a$ of 3b by UV/Vis spectroscopy**

![Graph of pH vs. Absorbance](image1)

**Figure S8. Left:** Dependence on pH of the absorption spectra of 62 µM solution of 3b from basic to acidic in 0.1M Britton-Robinson buffers. **Right:** Determination of $pK_a$ value of 3b by the sigmoidal fitting.

**Photocleavage / drug delivery of 5a/5b monitored by UV/Vis spectroscopy**

In a septum-sealed vial equipped with a magnetic stirrer 2.5 µmol of 5a/5b was dissolved in PBS buffer (2 mL, 0.01M, pH = 7.4) and the vessel was irradiated ($\lambda_{ex} = 455$ nm) in an intermittent manner while the LED was switched on/off every 2.5 min and 50 µL samples were taken in a 0.5 min interval for 13 min, filled up to 1 mL with 0.1M Britton-Robinson buffer (pH = 11.8) (63 µM) and measured.

![Graph of pH vs. Absorbance](image2)

**Figure S9.** Confirmation of drug delivery by UV absorption spectra of A) 5a and B) 5b after irradiation with visible light ($\lambda_{ex} = 455$ nm) in an off and on intermittent manner.
4. UV/Vis spectroscopy

**Figure S10.** UV/Vis spectra of the substrates 1a – g in 0.1M HCl/KCl buffer pH=2.1 and MeCN 9/1 (v/v) and 0.1M Britton-Robinson buffer pH=11.8 and MeCN 9/1 (v/v).
Table S1. Bathochromic shifts and molar attenuation coefficients of the substrates at different pH values.

| Substrate | $\lambda_{\text{max}}^{(1)}$ [nm] | $\varepsilon(\lambda_{\text{max}}^{(1)})$ [M$^{-1}$cm$^{-1}$] |
|-----------|----------------------------------|-------------------|
|           | pH = 2.1$^a$                     | pH = 11.8$^b$     |
| 1a        | 325                              | 4115              |
|           |                                  | 3184              |
| 1b        | 329                              | 6555              |
|           |                                  | 7173              |
| 1c        | 304                              | 3441              |
|           |                                  | 3667              |
| 1d        | 315                              | 4877              |
|           |                                  | 4913              |
| 1e        | 300                              | 2734              |
|           |                                  | 2475              |
| 1f        | 318                              | 2840              |
|           |                                  | 4339              |
| 1g        | 330                              | 7643              |
|           |                                  | 6701              |

UV/Vis spectra of 1a-g in $^a$0.1M HCl/KCl buffer pH=2.1 and MeCN 9/1 (v/v) and $^b$0.1M Britton-Robinson buffer pH=11.8 and MeCN 9/1 (v/v).
5. NMR Data

$^1$H NMR of 2-hydroxy-4-prop-2-ynyloxy-benzaldehyde S3

$^{13}$C NMR of 2-hydroxy-4-prop-2-ynyloxy-benzaldehyde S3
$^1$H NMR of propargyl-3-(2-hydroxy-4-(propargyloxy)phenyl)acrylate 1g

$^{13}$C NMR of propargyl-3-(2-hydroxy-4-(propargyloxy)phenyl)acrylate 1g
$^1$H NMR of coumarin 2a

![NMR spectrum of coumarin 2a](image)
$^1$H NMR of 7-hydroxycoumarin 2b
$^1$H NMR of 3-methylcoumarin 2c
$^1$H NMR of 3-methyl-7-hydroxycoumarin 2d
$^1$H NMR of 4-methylcoumarin 2e
$^1$H NMR of 3-allylcoumarin 2f
$^1$H NMR of 7-(propargyloxy)coumarin $2g$
$^1$H NMR of 3a
$^1$H NMR of 3b
$^1$H NMR of mPEG$_{2000}$-o-OH-benzaldehyde S6

$^{13}$C NMR of mPEG$_{2000}$-o-OH-benzaldehyde S6
$^1$H NMR of mPEG$_{2000}$-oHC-phenol 5a
$^1$H NMR of mPEG$_{2000}$-oHC-benzhydrol 5b
6. FTIR Data of 5a/5b
7. References

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