Supporting Information

Degradable Polyacetals/ketals from Alternating Ring-Opening Metathesis Polymerization

Benjamin R. Elling, Jessica K. Su, and Yan Xia*
Department of Chemistry, Stanford University, Stanford, California 94305, United States

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S1. Materials and Characterizations

S1.1. Materials All chemicals were purchased from commercial sources and used as received. CPEs **1a**[1a] and **1d**,[1b] acetal-type Dxps **2a-b**,[1c] and ketal-type Dxp **2c**[1d] were synthesized following the referenced literature procedures. Catalyst **G3** was synthesized by the literature procedure.[2] Unless otherwise specified, all CPE monomer syntheses were performed in flame-dried glassware under an atmosphere of N_2. Flash chromatography was performed using 230-400 mesh, grade 60 silica gel.

S1.2. Characterizations ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ using 300 MHz, 400 MHz, 500 MHz, or 600 MHz Varian NMR spectrometers. Chemical shifts are reported in ppm relative to residual protonated solvent for ^{1}H ($CHCl_3$ = δ 7.26) and relative to carbon resonances of the solvent for ^{13}C ($CDCl_3$ δ = 77.0). GPC was performed in THF on two PLgel 10 *μ*m mixed-B LS columns (Agilent Technologies) connected in series with a DAWN 8+ multiangle laser light scattering (MALLS) detector and an Optilab T-rEX differential refractometer (both from Wyatt Technology). No calibration standards were used, and d*n*/d*c* values were obtained by assuming 100% mass elution from the columns. HPLC-MS was performed in acetonitrile/water containing 0.1% formic acid on an Alliance e2695 Separations Module using an XBridge 3.5 *μ*m 2.1x50 mm C18 column in series with a 2489 UV/Visible Detector and an Acquity QDa Detector (Waters Corporation).

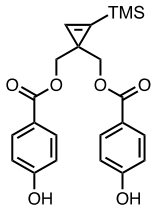
S2. Experimental Procedures

S2.1. Procedure for AROMP The desired amounts of CPE monomers were added in vials equipped with a stir bar under an N_2 atmosphere. Dry, degassed THF was then added to the vials. Stock solutions of Dxp and catalyst **G3** were prepared in THF, and the required amounts of Dxp, followed by catalyst, were injected to each vial to begin polymerization at room temperature. Conversion was monitored by taking aliquots from the solution, which were quenched with a few drops of ethyl vinyl ether, concentrated *in vacuo*, and analyzed by ^{1}H NMR spectroscopy. Upon completion of the polymerization, the reactions were terminated by the addition of a few drops of ethyl vinyl ether. The resulting polymers were isolated by precipitating into MeOH (or Et_2O in the case of poly(**1c**-*alt*-**2a**)), concentrating by centrifugation, and drying under vacuum.

S2.2. Procedure for Block Copolymer Synthesis via AROMP 75 equiv of **1a** were added to vials equipped with a stir bar under an atmosphere of N_2. The requisite amount of dry, degassed THF was added to the vials to give a 0.3 M **1a** solution. Stock solutions of Dxp and catalyst were prepared in THF, then 25 equiv of Dxp and 1 equiv of catalyst **G3** were injected to each vial to begin polymerization at room temperature. After ~6 h of polymerization, the solution was diluted to give a 0.1 M solution of **1a**. Finally, 500 equiv of cyclohexene (CHex) were added and an aliquot of the crude reaction mixture taken to acquire a GPC chromatogram. After 6 h, the reactions were terminated by the addition of a few drops of ethyl vinyl ether. The resulting polymers were isolated by precipitating into MeOH.

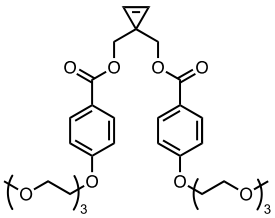
S2.3. Procedure for Polymer Degradation In a 1-dram vial equipped with a stir bar was dissolved 4 mg of the isolated polymer in 1 mL THF. To the stirred polymer solution was added 10 µL of TFA to induce degradation (an equivalent amount of acetic acid was only able to degrade the polyketal relatively slowly). Aliquots of the solution were taken at different time points to monitor the crude degraded polymers by GPC.

S2.4. Monomer Syntheses



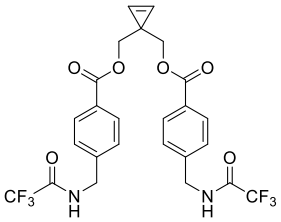
(2-(Trimethylsilyl)cycloprop-2-ene-1,1-diyl)bis(methylene) bis(4-hydroxybenzoate) (S1)

To a flame-dried 50-mL round bottom flask were added 4-(methoxymethoxy)benzoic acid (0.93 g, 5.1 mmol), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (1.2 g, 7.7 mmol), and 4-dimethylaminopyridine (60 mg, 0.5 mmol) under an atmosphere of N_2. The mixture was dissolved in dry DCM (15 mL), to which (2-(trimethylsilyl)cycloprop-2-ene-1,1-diyl)dimethanol[1a] (441 mg, 2.6 mmol) in dry DCM (5 mL) was added. The reaction mixture was allowed to stir at room temperature for 48 hours. Then, the solution was extracted with sat. NH_4Cl (aq.) and the organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography (30% ethyl acetate in hexanes) to afford (2-(trimethylsilyl)cycloprop-2-ene-1,1-diyl)bis(methylene) bis(4-(methoxymethoxy)benzoate) (635 mg, 50%) as a colorless oil. Following its isolation, the MOM-protected intermediate was added to a 20-mL scintillation vial in a mixture of methanol and acetone (~10 mL) under ambient conditions. 1M HCl (1 mL) and two drops of conc. HCl were added to the reaction mixture, which was stirred overnight at 55 °C. The solution was then extracted with ethyl acetate, and the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by flash column chromatography (50% ethyl acetate in hexanes) to afford (2-(trimethylsilyl)cycloprop-2-ene-1,1-diyl)bis(methylene) bis(4-hydroxybenzoate) (**S1**) (326 mg, 62%) as a white solid. ^{1}H NMR (400 MHz, $(CD_3)_2CO$): δ -0.25 (s, 9 H), 2.93 (s, 4 H), 3.77-3.89 (q, 4 H, J = 11.36 Hz), 6.39-6.41 (d, 4 H, J = 8.72 Hz), 7.38-7.40 (d, 4 H, J = 8.68 Hz), 7.76 (s, 1 H), 9.91 (s, 2 H). ^{13}C NMR (100 MHz, $(CD_3)_2CO$): δ -1.02, 25.00, 72.13, 116.15, 122.95, 126.55, 128.81, 162.70, 166.66. ESI-MS m/z calc. for fragment $C_{15}H_{18}O_3Si$ $[M]^{\bullet+}$: 275.4; found: 275.0.



Cycloprop-2-ene-1,1-diylbis(methylene)bis(4-(2-(2-(2 methoxyethoxy)ethoxy)ethoxy) benzoate (1b)

To a flame-dried 50-mL round bottom flask were added **S1** (250 mg, 0.6 mmol), 2-(2-(2-methoxyethoxy)ethoxy)ethyl 4-methylbenzenesulfonate (386 mg, 1.2 mmol), and potassium carbonate (331 mg, 2.4 mmol) under an atmosphere of N_2. The mixture was dissolved in dry acetonitrile (10 mL), and stirred at reflux temperature for 48 h. The solution was concentrated *in vacuo* and purified by silica gel column chromatography (100% ethyl acetate) to afford cycloprop-2-ene-1,1-diylbis(methylene) bis(4-(2-(2-(2-methoxyethoxy)ethoxy)ethoxy)benzoate) (**1b**) as a colorless oil (150 mg, 39%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.38 (s, 6 H), 3.52-3.72 (m, 16 H), 3.85-3.92 (t, *J* = 4.9 Hz, 4 H), 4.15-4.18 (t, *J* = 4.9 Hz, 4 H), 4.37 (s, 4 H), 6.86-6.95 (d, *J* = 8.7 Hz, 4 H), 7.34 (s, 2 H), 7.93-8.02 (d, *J* = 8.9 Hz, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 59.1, 67.5, 69.5, 70.2, 70.6, 70.7, 70.9, 71.9, 112.8, 115.5, 116.7, 121.2, 129.5, 162.8. ESI-MS m/z calc. for fragment $C_{19}H_{24}O_6$ $[M]^{\bullet+}$: 349.4; found: 349.1.



Cycloprop-2-ene-1,1-diylbis(methylene) bis(4-((2,2,2-trifluoroacetamido)methyl)benzoate) (1c)

To a flame-dried 25-mL round bottom flask were added 4-((2,2,2-trifluoroacetamido)methyl)benzoic acid[3] (0.85 g, 3.2 mmol), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (0.75 g, 4.8 mmol), and 4-dimethylaminopyridine (40 mg, 0.3 mmol) under an atmosphere of N_2. The mixture was dissolved in dry DCM (13 mL), to which (2-(trimethylsilyl)cycloprop-2-ene-1,1-diyl)dimethanol[1a] (276 mg, 1.6 mmol) in dry DCM (2 mL) was added. The reaction mixture was allowed to stir at room temperature for 24 hours. The solution was washed with 25 mL water, then extracted twice into 50 mL DCM. The organic fractions were washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (R_f = 0.50, 10% MeOH in DCM) to afford **1c-TMS** (643 mg, 64%) as a white solid. **1c-TMS** in 3mL THF was subsequently added to a flame-dried 25-mL round bottom flask under N_2 gas at -78°C. TBAF (1.0 M in THF with ~5% H_2O, 0.89 mL, 0.8 mmol) was added to the solution, which was then allowed to warm to room temperature over 1 h with stirring. The mixture was then added to a silica gel column and flushed with a solution of 10% MeOH in EtOAc to give **1c** (500 mg, 87%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.45 (s, 4 H), 4.55 (d, *J* = 6.2 Hz, 4 H), 7.10 (bs, 2 H), 7.20 (d, *J* = 7.9 Hz, 4 H), 7.41 (s, 2 H), 7.93 (d, *J* = 7.8 Hz, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 42.7, 71.3, 116.1, 127.3, 129.0, 130.2, 139.0, 165.5. ESI-MS m/z calc. for fragment $C_{15}H_{12}F_3NO_3$ $[M]^{\bullet+}$: 312.3; found: 312.0.

S2.5. Polymer ^{1}H NMR Data

Poly(1a-*alt*-2a) ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.84 – 0.56 (m, 3H), 1.47 (m, 2H), 4.13 – 3.78 (m, 4H), 4.38 (m, 5H), 5.89 – 5.50 (m, 4H), 7.33 (m, 4H), 7.46 (m, 2H), 8.00 – 7.79 (m, 4H).

Poly(1a-*alt*-2b) ^{1}H NMR (600 MHz, $CDCl_3$): δ 4.16 – 3.65 (m, 4H), 4.40 (m, 4H), 5.95 – 5.36 (m, 5H), 7.26 (m, 9H), 7.48 (m, 2H), 7.92 (m, 4H).

Poly(1a-*alt*-2c) ^{1}H NMR (600 MHz, $CDCl_3$): δ 1.35 – 1.10 (m, 6H), 3.48 (m, 2H), 4.09 – 3.78 (m, 4H), 4.56 – 4.26 (m, 4H), 5.89 – 5.53 (m, 4H), 7.43 – 7.27 (m, 4H), 7.49 (m, 2H), 8.09 – 7.82 (m, 4H).

Poly(1b-*alt*-2a) ^{1}H NMR (600 MHz, $CDCl_3$): δ 0.80 (m, 3H), 1.59 – 1.39 (m, 2H), 3.36 (s, 5H), 3.53 (m, 3H), 3.78 – 3.60 (m, 9H), 3.85 (m, 3H), 4.27 – 3.91 (m, 7H), 4.42 (m, 5H), 5.95 – 5.61 (m, 4H), 6.88 (m, 4H), 7.91 (m, 4H).

Poly(1c-*alt*-2a) ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.71 (s, 3H), 1.42 (s, 2H), 4.79 – 4.23 (m, 8H), 5.73 (s, 4H), 7.15 (s, 4H), 7.76 (s, 4H), 8.37 (s, 2H).

Poly(1d-*alt*-2a) ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.78 (m, 3H), 1.31 – 1.20 (m, 2H), 4.46 (s, 4H), 4.56 (s, 4H), 5.77 (m, 4H), 7.41 (m, 6H), 7.95 (m, 4H).

S3. Supplemental Figures and Tables

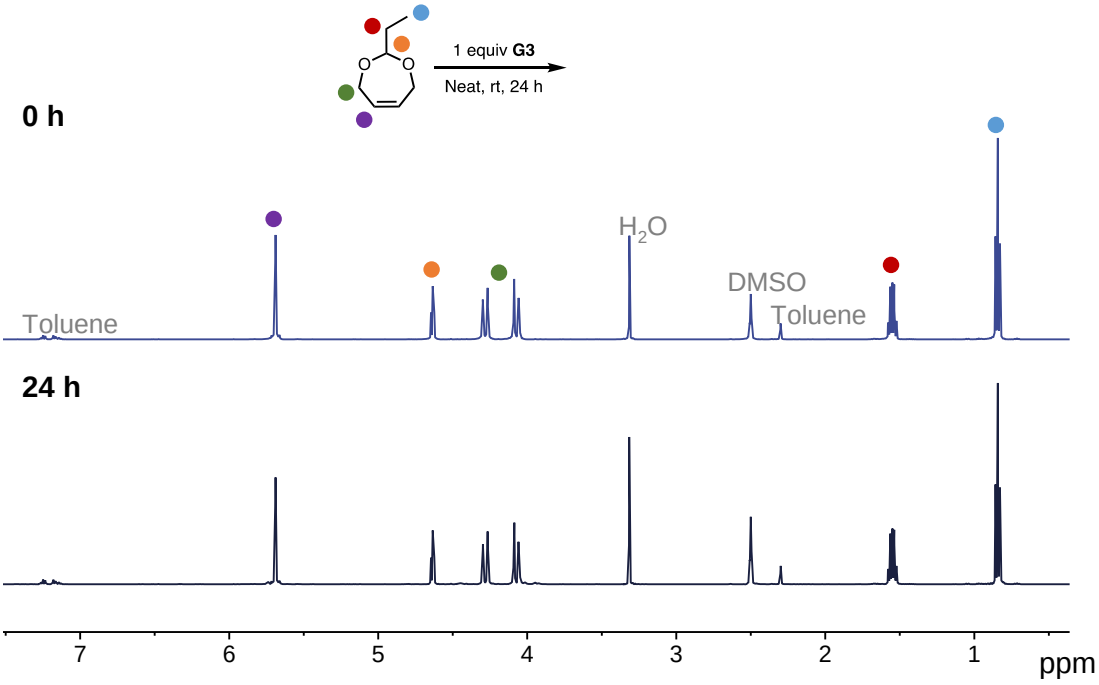


Figure S1. ^{1}H NMR spectra of Dxp **2a** and **G3** (500:1) after 0 h and 24 h at room temperature under N_2, showing its negligible oligomerization.

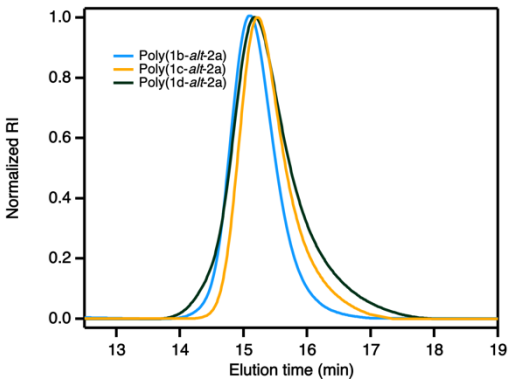


Figure S2. GPC traces of poly(**1b**-*alt*-**2a**), poly(**1c**-*alt*-**2a**), and poly(**1d**-*alt*-**2a**) (Table 1, entries 10-12).

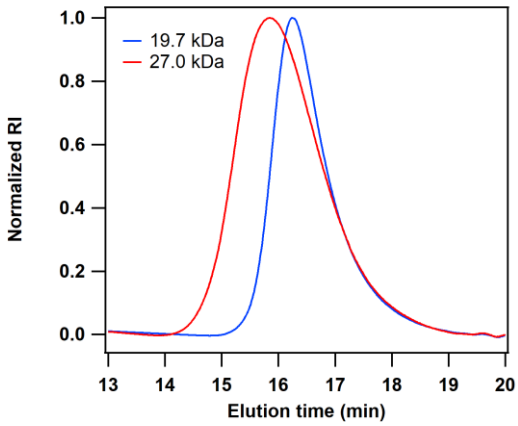


Figure S3. Additional GPC traces of poly(**1a**-*alt*-**2a**) targeting higher MWs (Table 1, entries 5-6).

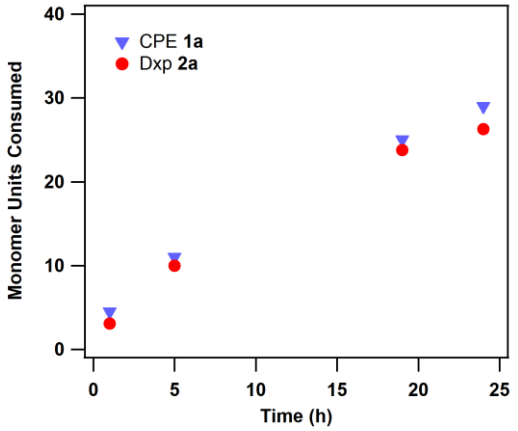


Figure S4. Plot of monomer units consumed of CPE **1a** (blue) and Dxp **2a** (red) vs time during their copolymerization. Conditions: [**1a**]$_0$ = 0.1 M, [**2a**]$_0$/[**1a**]$_0$ = 1.25, [**1a**]$_0$/[**G3**]$_0$ = 50:1, $CDCl_3$, room temperature. The ratio of **1a:2a** in poly(**1a**-*alt*-**2a**) remained close to 1:1 throughout the copolymerization, suggesting a mainly alternating sequence.

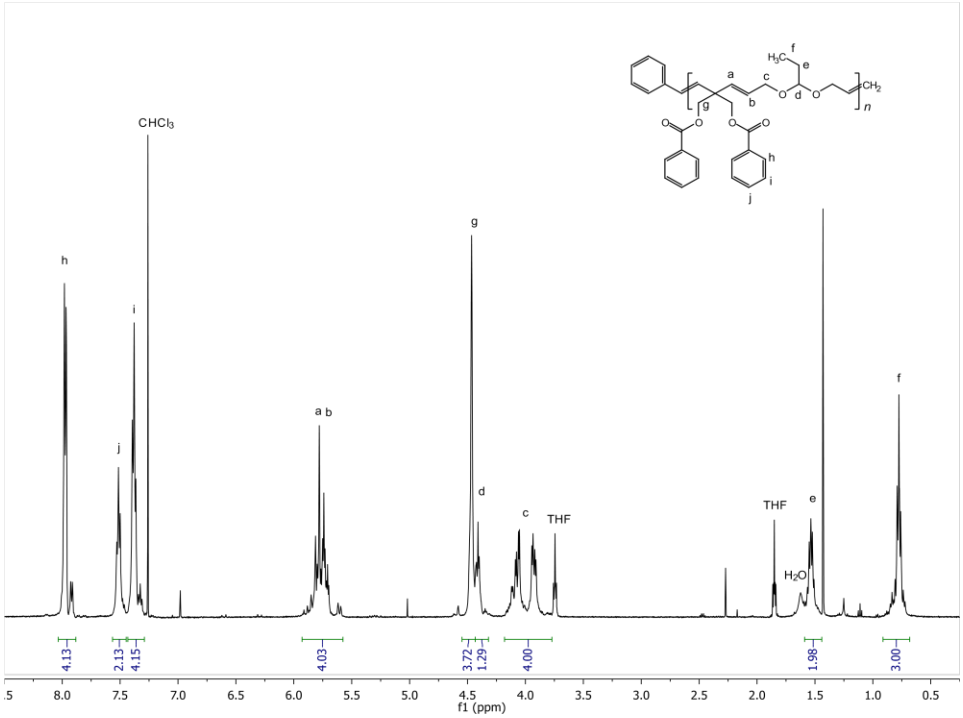


Figure S5. Assigned ^{1}H NMR spectrum of poly(**1a**-*alt*-**2a**) (Table 1, entry 4).

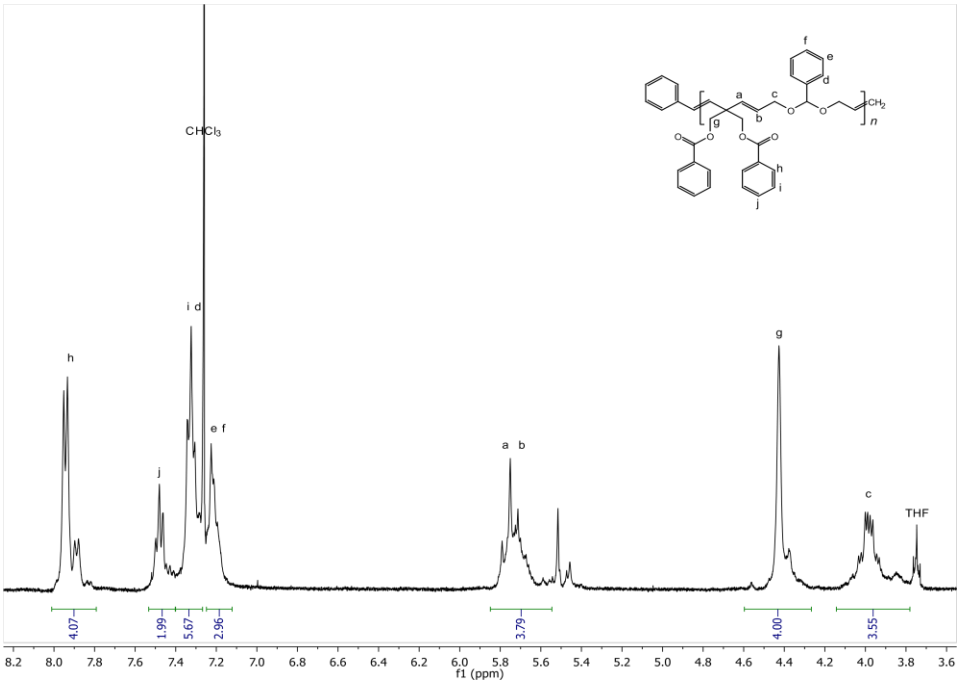


Figure S6. Assigned ^{1}H NMR spectrum of poly(**1a**-*alt*-**2b**) (Table 1, entry 7).

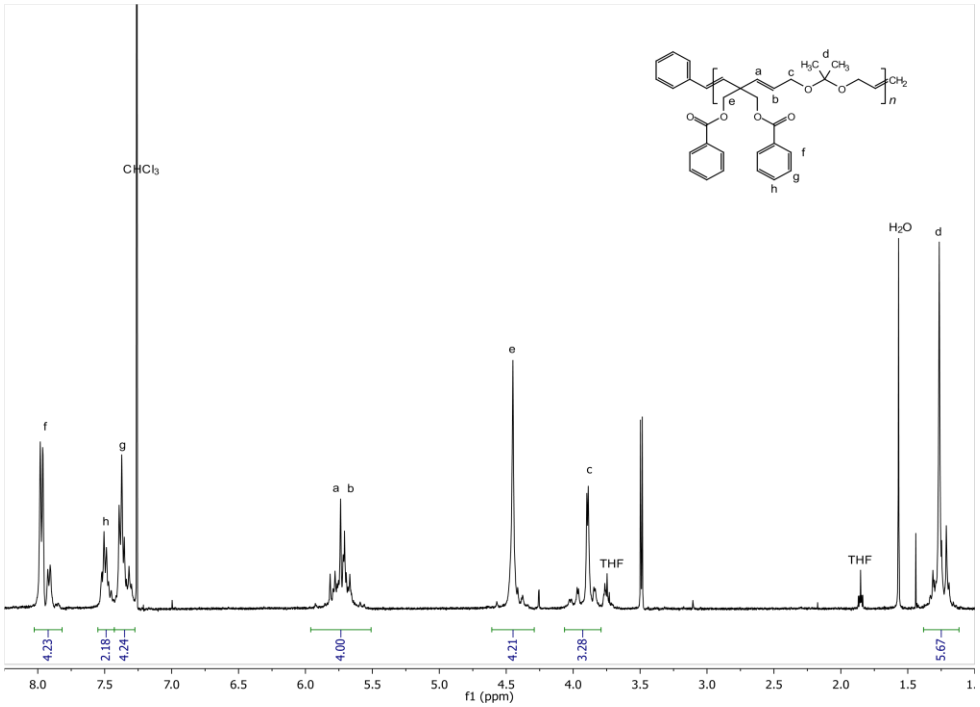


Figure S7. Assigned ^{1}H NMR spectrum of poly(**1a**-*alt*-**2c**) (Table 1, entry 9).

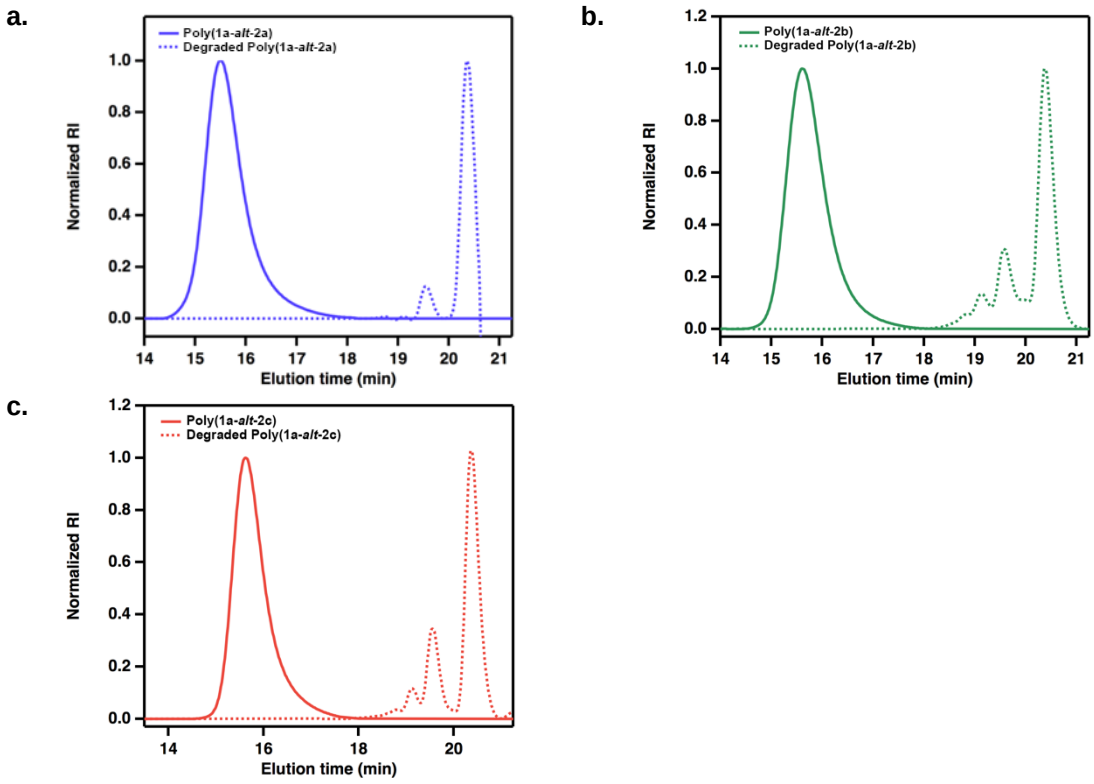
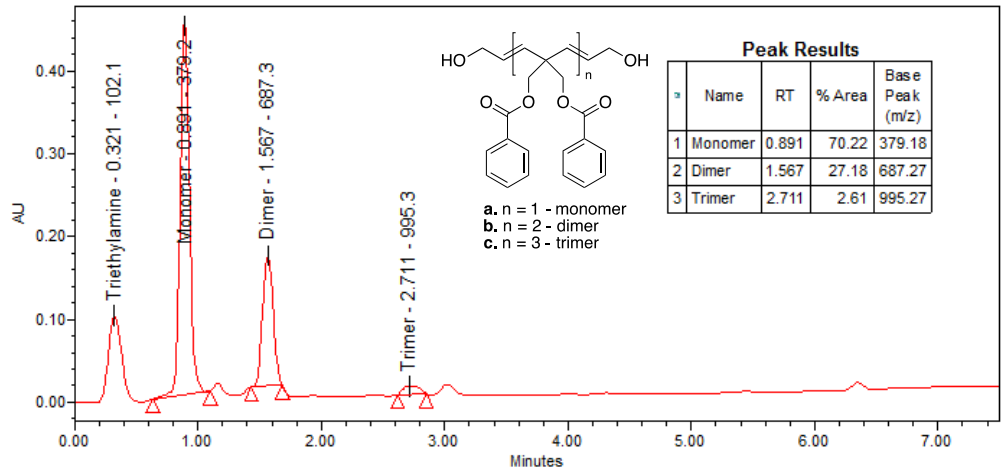


Figure S8. GPC traces of (a) poly(**1a**-*alt*-**2a**) (Table 1, entry 4), (b) poly(**1a**-*alt*-**2b**) (Table 1, entry 7), and (c) poly(**1a**-*alt*-**2c**) (Table 1, entry 9) before and after backbone hydrolysis, showing complete polymer degradation.

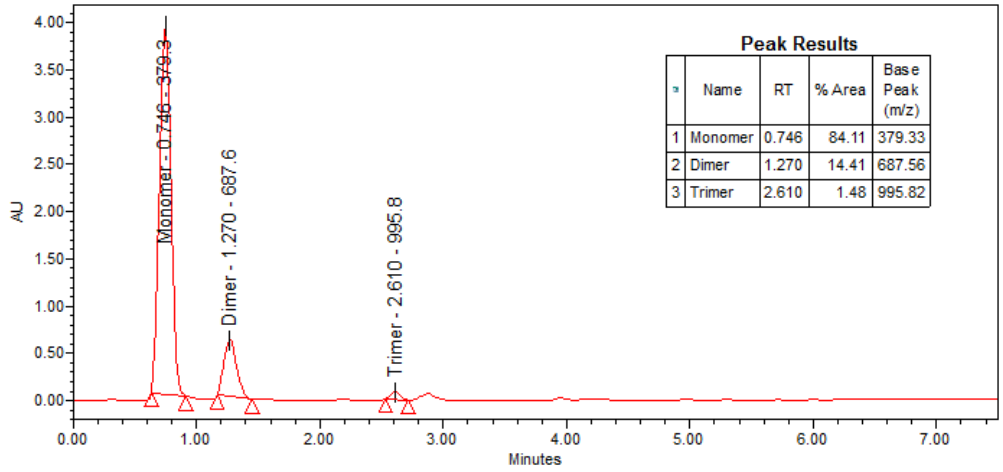
a.



Peak Results

	Name	RT	% Area	Base Peak (m/z)
1	Monomer	0.891	70.22	379.18
2	Dimer	1.567	27.18	687.27
3	Trimer	2.711	2.61	995.27

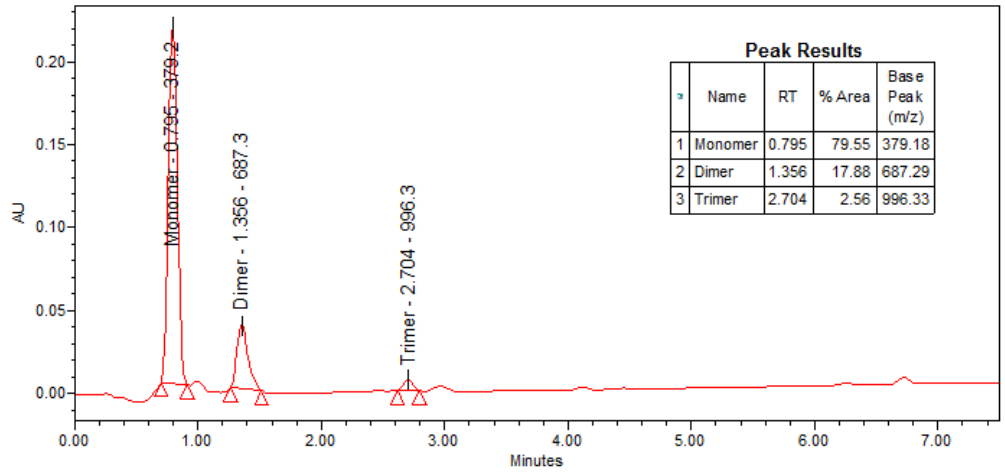
b.



Peak Results

	Name	RT	% Area	Base Peak (m/z)
1	Monomer	0.746	84.11	379.33
2	Dimer	1.270	14.41	687.56
3	Trimer	2.610	1.48	995.82

c.



Peak Results

	Name	RT	% Area	Base Peak (m/z)
1	Monomer	0.795	79.55	379.18
2	Dimer	1.356	17.88	687.29
3	Trimer	2.704	2.56	996.33

Figure S9. HPLC chromatograms (UV detector at 254 nm) of the degradation products of (a) poly(**1a**-*alt*-**2a**), (b) poly(**1a**-*alt*-**2b**), and (c) poly(**1a**-*alt*-**2c**) (Table 1, entries 4, 7, and 9) after treatment with TFA in THF. Retention time, % area, and molecular mass of each peak are listed in the inserted table.

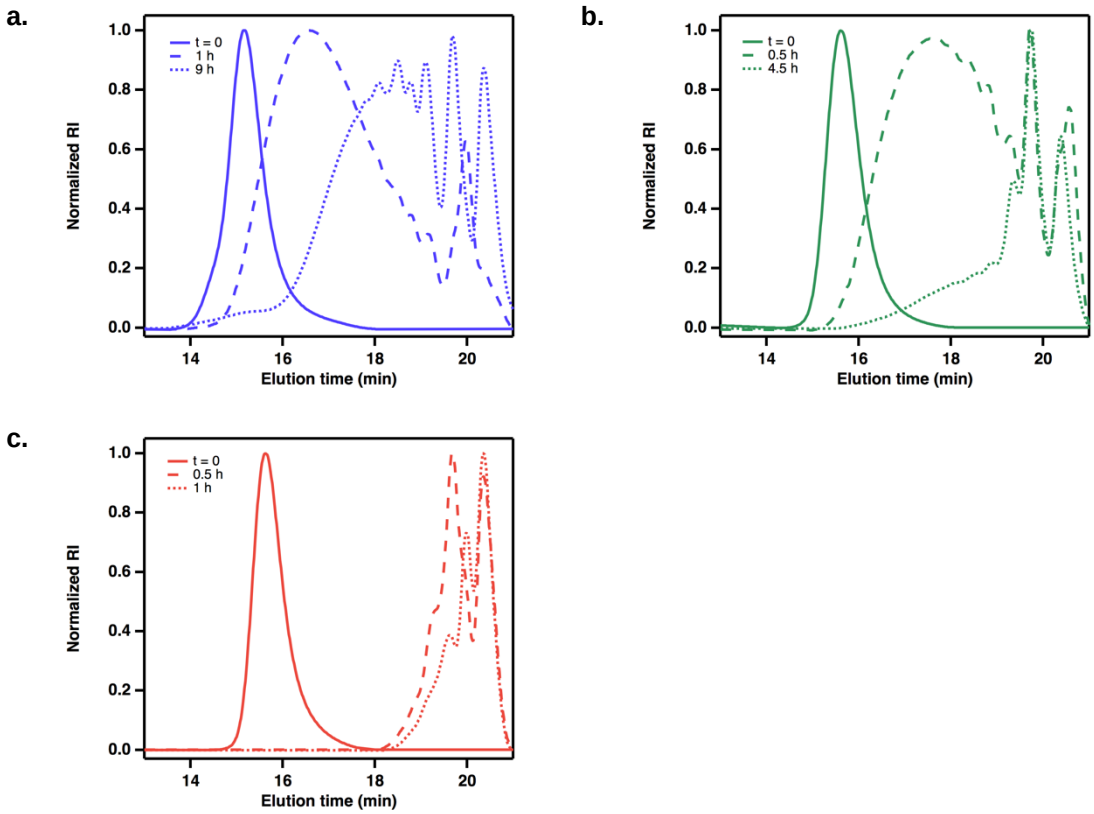


Figure S10. Degradation profiles of polyacetals/ketal: GPC traces of (a) poly(**1a**-*alt*-**2a**), (b) poly(**1a**-*alt*-**2b**), and (c) poly(**1a**-*alt*-**2c**) (Table 1, entries 4, 7, and 9) at different time points during degradation with TFA.

Table S1. Synthesis of Block Copolymers

Entry	Dxp	Block 1 M_n[a] (kDa)	Block 1 $Đ_M$	Diblock M_n[a] (kDa)	Diblock $Đ_M$
1	**2a**	9.7	1.04	24.9	1.07
2	**2b**	15.5	1.05	27.9	1.09
3	**2c**	12.7	1.04	25.1	1.09

[a] Determined by GPC-MALLS analysis in THF. Block 1 = poly(**1a**-*alt*-**2**); diblock = poly(**1a**-*alt*-CHex)-*b*-poly(**1a**-*alt*-**2**).

S4. Additional NMR Spectra

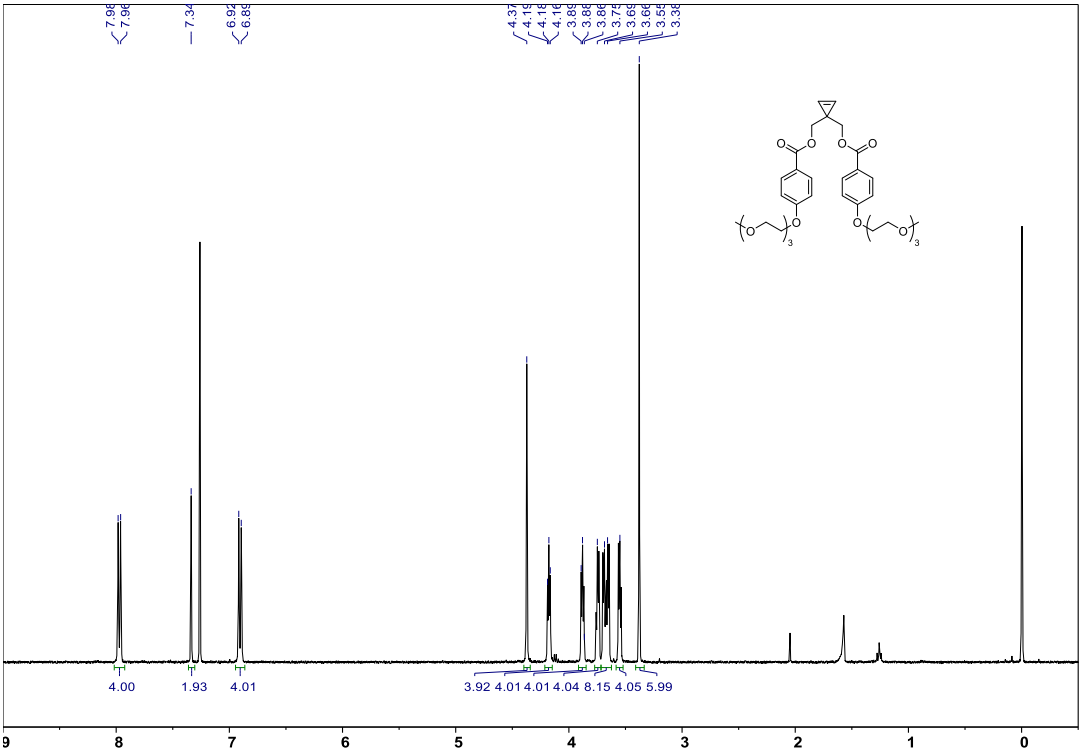


Figure S11. ^{1}H NMR spectrum of **1b**.

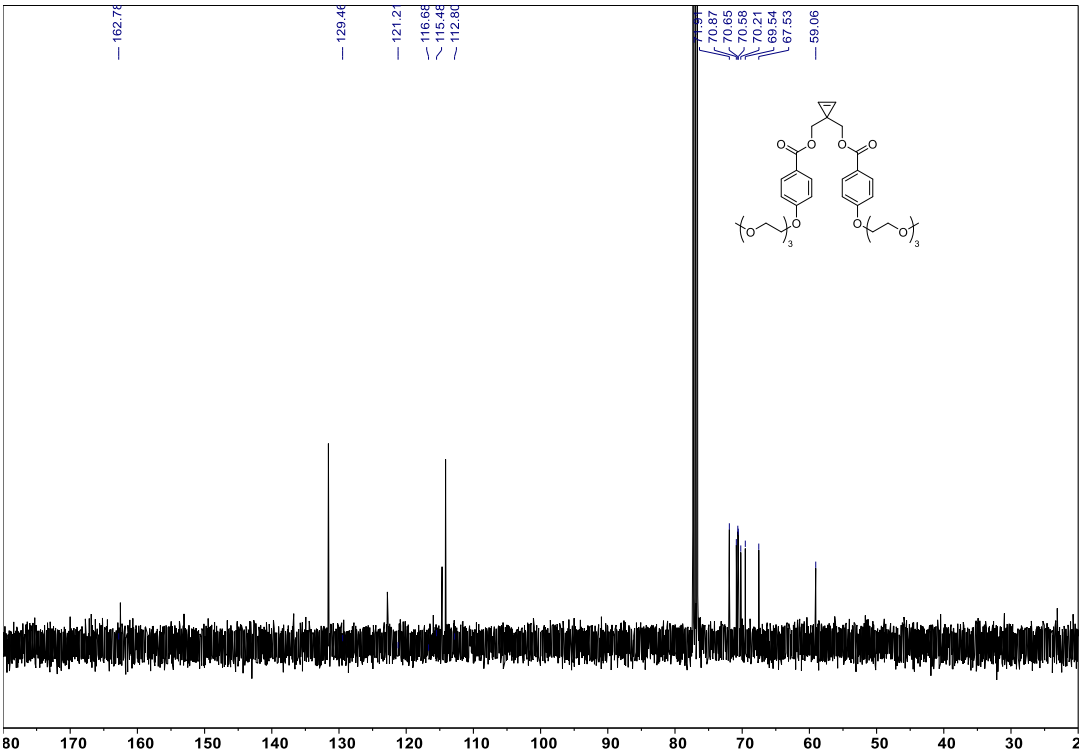


Figure S12. ^{13}C NMR spectrum of **1b**.

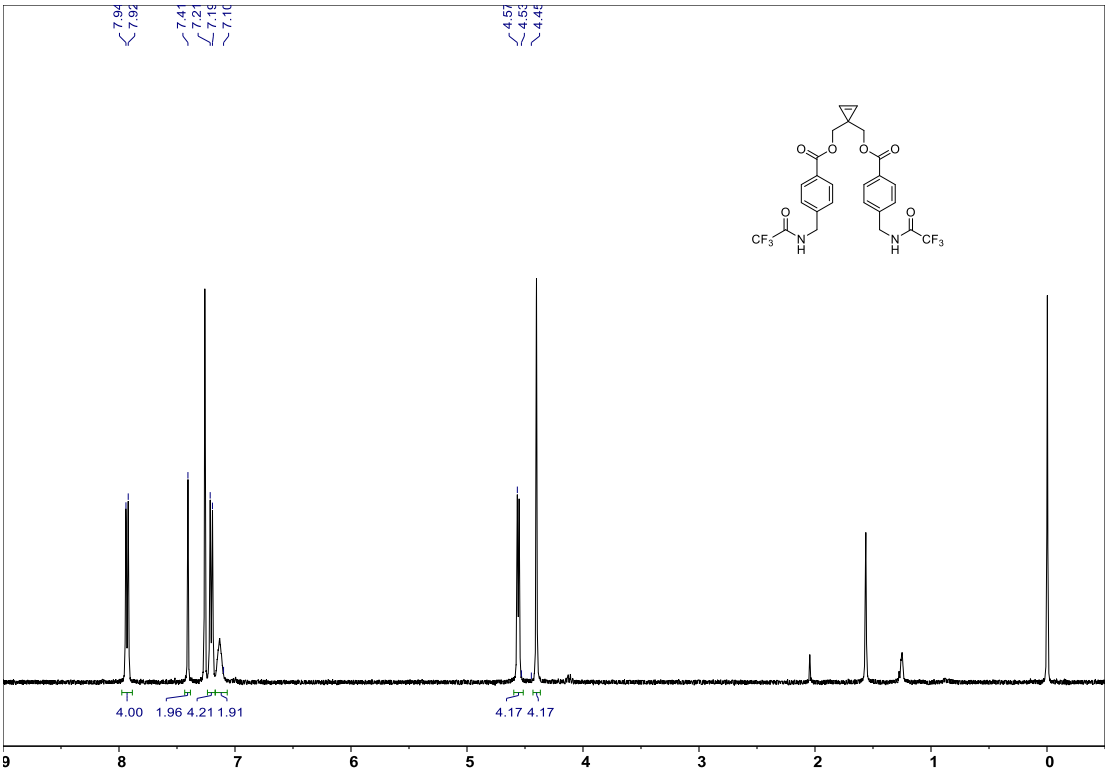


Figure S13. ^{1}H NMR spectrum of **1c**.

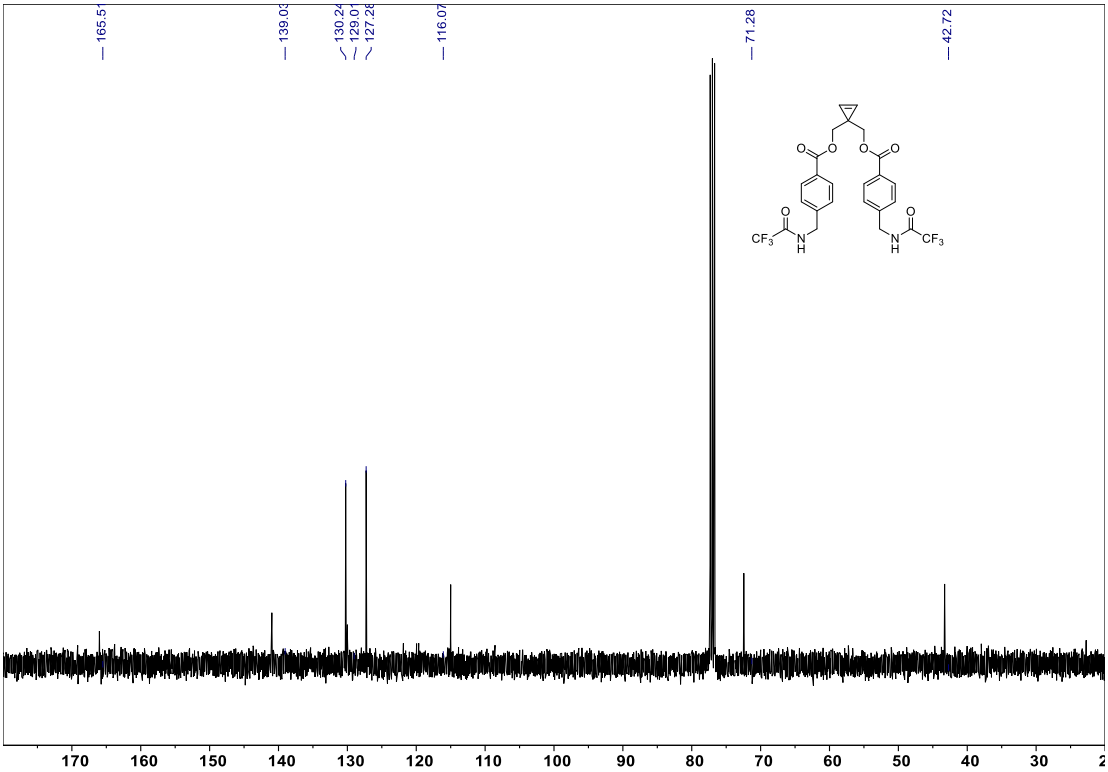


Figure S14. ^{13}C NMR spectrum of **1c**.

S5. Supplemental References

(1) (a) Krämer, K.; Leong, P.; Lautens, M. Enantioselective Palladium-Catalyzed Carbozincation of Cyclopropenes. *Org. Lett.* **2011**, *13*, 819; (b) Elling, B. R.; Xia, Y. Efficient and Facile End Group Control of Living Ring-Opening Metathesis Polymers via Single Addition of Functional Cyclopropenes. *ACS Macro Lett.* **2018**, *7*, 656; (c) Ogata, Y.; Masson, G.; Hishiro, Y.; Blackwell, J. M. Scissionable Polymer Resists for Extreme Ultra-Violet Lithography. *Proc. SPIE* **2010** 10.1117/12.847320; (d) Szpera, R.; Kovalenko, N.; Natarajan, K.; Paillard, N.; Linclau, B. The Synthesis of the 2,3-difluorobutan-1,4-diol diastereomers. *Beilstein J. Org. Chem.* **2017**, *13*, 2883.

(2) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H. A Practical and Highly Active Ruthenium-Based Catalyst that Effects the Cross Metathesis of Acrylonitrile. *Angew. Chem. Int. Ed.* **2002**, *41*, 4035.

(3) Alam, S.; Alves, D. S.; Whitehead, S. A.; Bayer, A. M.; McNitt, C. D.; Popik, V. V.; Barrera, F. N.; Best, M. D. A Clickable and Photocleavable Lipid Analogue for Cell Membrane Delivery and Release. *Bioconjugate Chem.* **2015**, *26*, 1021.