

## Organocatalysis in Ring Opening Copolymerization as a Means of Tailoring Molecular Weight Dispersity and the Subsequent Impact on Physical Properties in 4D Printable Photopolymers

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## Experimental Section

*General:* All chemicals and materials were purchased from Sigma-Aldrich and used without further purification unless otherwise noted. The following instrumentation was used to analyze and characterize each of the synthesized polyesters: SEC was conducted using HPLC grade chloroform as the mobile phase on an Agilent 1100 HPLC system with a 300 mm  $\mu$ L-Gel mixed C and a 250 mm PLgel miniMix-D dual column setup at room temperature (25 °C) with results calculated by Cirrus SEC software against polystyrene standards;  $^1\text{H}$  nuclear magnetic resonance (NMR) spectra were recorded at room temperature (25 °C, 298 K) on a 500 MHz Bruker spectrometers with shifts reported in parts per million and referenced against the residual deuterated chloroform peak with analysis conducted using MestReNova software v14.2.2; mechanical analyses were conducted *via* an Instron tensiometer equipped with a 100 kg load cell; Differential scanning calorimetry (DSC) was performed with a TA instruments Q 2000 to explore the migration of the glass transition temperature ( $T_g$ ) for the poly(CHA-co-AGE) polyester synthesized with different catalysts over various time points;

*ROCOP of cyclohexene anhydride and allyl glycidol ether:* All polymerizations were performed in sealed glass vials in bulk under ambient atmosphere, with all experiments conducted at 100 °C over 48 hours.<sup>1-5</sup> Organic catalysts 1H-pyrazolo[3,4- $\beta$ ]pyridine, 1H-pyrrolo[2,3- $\beta$ ]pyridine, and 1,1,3,3-tetramethylguanidine were tested individually as well as with the co-catalyst/initiators N-(p-tolyl)thiourea, N,N'-diphenylthiourea, and propargyl alcohol. The syntheses were performed at the 5 g. scale with a 1 to 1 stoichiometric ratio of anhydride to epoxide. A general example of the reaction is as follows; 2.86 g (0.019 mol) CHA, was combined with 2.14 g (0.019 mol) AGE and 11.20 mg (0.094 mmol) pyr34 catalyst in a glass vial, which was sealed and placed into an oven at 100 °C for 48 hours. Aliquots were taken at 1, 3, 6, 12, 24, and 48 hours to monitor the reaction progression.

*Polymerization kinetics:* The progress of the reaction was monitored by analyzing  $^1\text{H}$  NMR spectra and SEC traces. Aliquots at 1, 3, 6, 12, 24, and 48 hours were collected and quenched in acetic acid.<sup>6</sup> Monomer conversion was determined for each of the aliquots by  $^1\text{H}$  NMR spectroscopy comparing the integration of the  $-\text{CH}_2$  peak of the closed epoxide at  $\sim 2.72$  ppm with the corresponding  $-\text{CH}_2$  peak of the opened epoxide incorporated into the poly(CHA-co-AGE) polyester backbone at  $\sim 4.37$  ppm. SEC was performed on each aliquot to determine the potential relationship between molecular weight and dispersity, with polymerization time and catalyst/initiator species utilized. The number average molecular weight by NMR was determined by comparing the integration of the end group of the poly(CHA-co-AGE) polyester with the  $\text{CH}_2$  of the opened allyl glycidyl ether..

*Fluorometry:* Purified polyesters and commercially available monomers were dissolved in acetone and were analyzed for fluorescence emission/excitation behaviors using a Horiba Instruments Fluorolog 3 fluorometer. The behaviors were briefly optimized using excitation behavior, followed by emission behavior determination that was used for subsequent excitation. The resultant intensity counts per second of the excitation and emission spectra were normalized for comparison across formulations. A DBU-catalyzed polyester (no initiator) was used as a non-fluorescing polymer. Emission peak wavelengths and full width half maxima were calculated for each species.

*Rheology:* Poly(CHA-co-AGE) polyesters ( $\sim 10$  kDa by SEC) of differing dispersities were further compared *via* rheology to probe differences in viscosity as the dispersity of the polyester changes. These polyesters were analyzed for viscosity with a TA instruments DHR-3 rheometer with a parallel Peltier plate system. The 40 mm parallel plate geometry, with a 500  $\mu\text{m}$  gap at ambient temperature (25 °C), was used

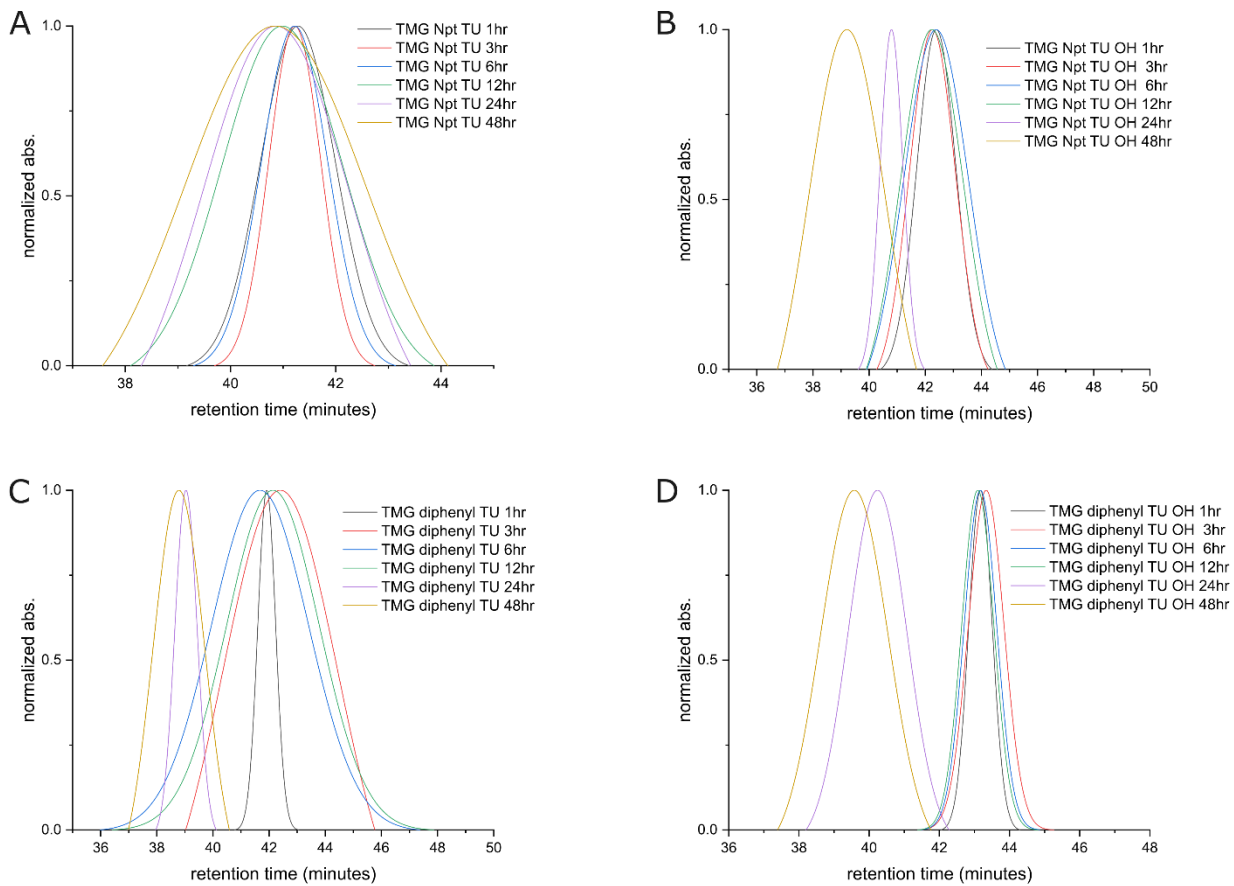
to subject the samples to a shear rate ramping from 0.2 to 2000 rpm, following protocols published by Merckle.<sup>7,8</sup>

*Photopolymer resin:* Photoreactive resin was produced by combining the poly(CHA-co-AGE) with pentaerythritol tetra(3-mercaptopropionate) (PETMP) in a stoichiometric ratio of thiol groups of PETMP to alkene groups of the poly(CHA-co-AGE) polyester repeat unit. Additionally, the photoinitiator Irgacure 819 was a mass of 0.5 wt% to each resin. A representative protocol for the production of the resin is as follows; 4.00 g., 0.015 mol poly(CHA-co-AGE) is mixed to homogeneity with 3.67 g., 0.0075 mol PETMP. 2.00 g. acetone was added to homogenize the components and dissolve the photoinitiator, Irgacure 819 (0.038 g., 0.09 mmol), which is added at this point. The resin was allowed to mix overnight in an open container to remove residual solvent. The resultant resin was printed *via* an Elegoo MARS DLP printer.

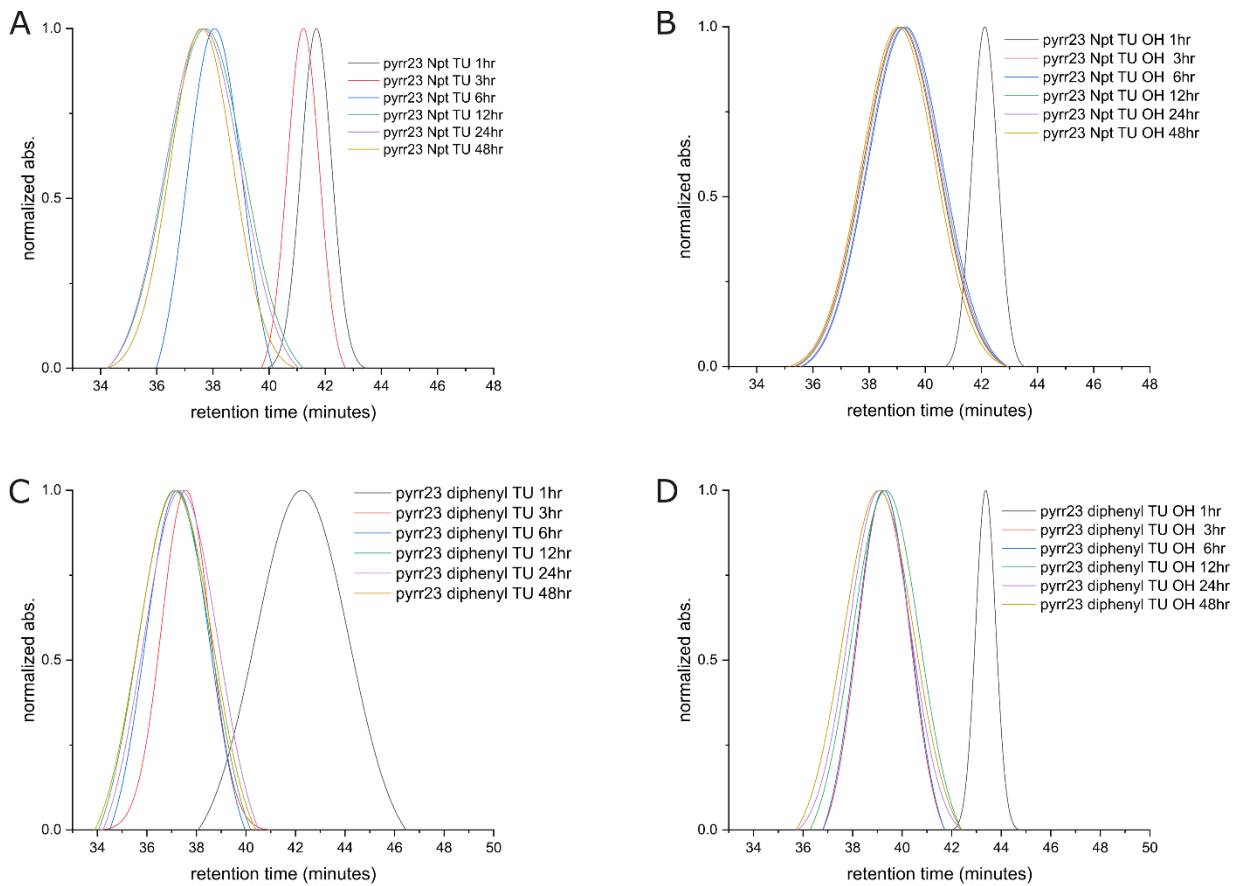
*Digital light processing 3D printing:* To the ~8 g of photoreactive resin (from the *Photopolymer resin* method above) was added 200  $\mu$ l of a mixture of the photo inhibitor lutein (0.99 g.) and acetone (0.70 g) was added to the photoresin to act as an inhibitory agent to prevent overcuring of the resin when exposed to the 405 nm light. The scaffold structure was created using CAD software and sliced with Chitubox software V1.9.0 and the final product was printed with an Elegoo MARS with a layer height of 0.07 mm and an exposure time of 20 seconds per slice.

*Mechanical testing:* Using an Instron tensiometer equipped with a 100 kg load cell, 3D printed ASTM type IV dogbones were uniaxially tested until failure at a rate of 10 mm x min<sup>-1</sup>. Resulting data was analyzed for comparisons between elastic modulus, strain at break, ultimate tensile strength, and toughness of the poly(CHA-co-AGE) polyesters of varying dispersities.

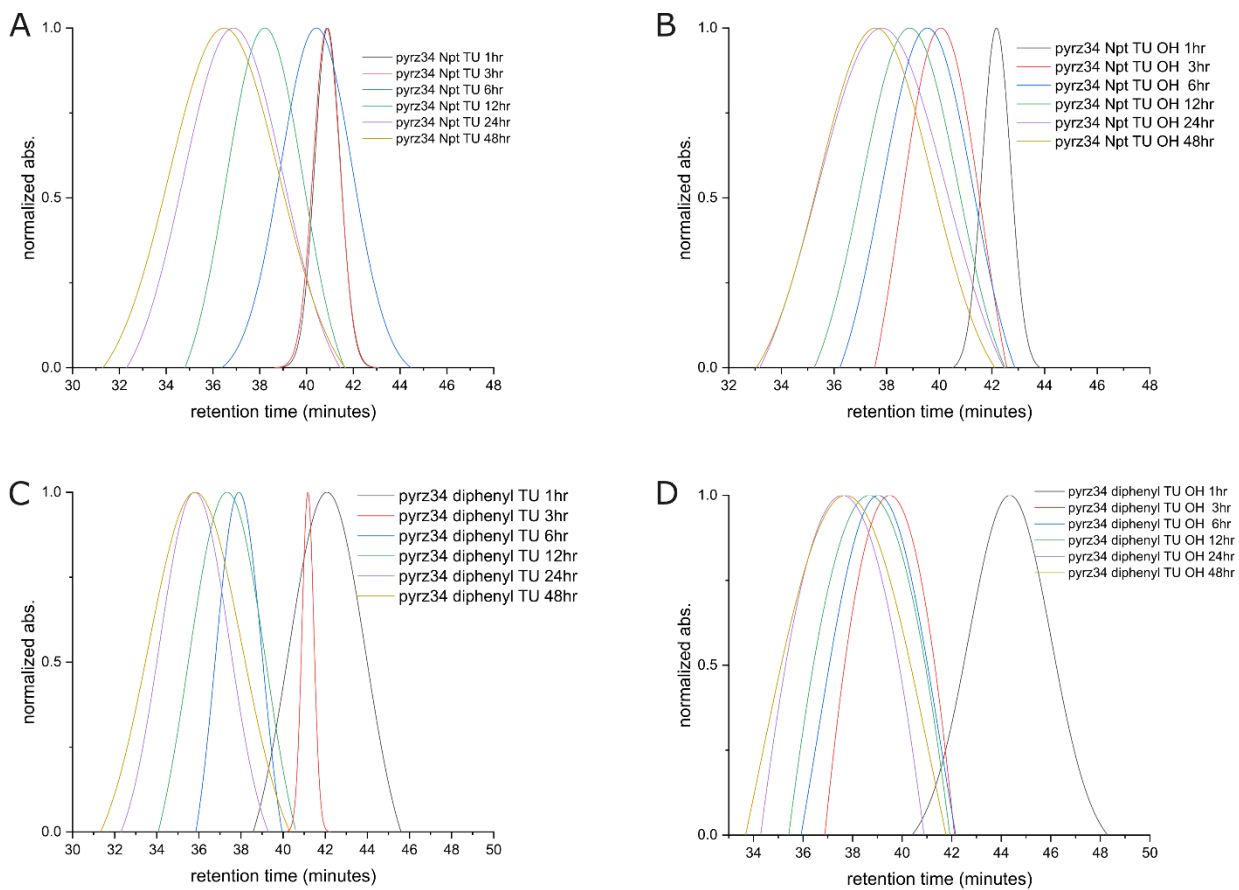
*Thermal analysis:* ~10 mg. of each dispersity sample of poly(CHA-co-AGE) was subjected to DSC analysis to determine the effect that dispersity has on the glass transition temperature of the polyester. Samples were placed in aluminum pans and cooled to -90 °C, where they were held for 5 minutes, before ramping to 200 °C at a rate of 10 °C x min<sup>-1</sup> with the cooling and heating cycles repeated twice more. The  $T_g$  values were calculated from the final heating cycle, taking the mid-point of the step transition on the thermogram..



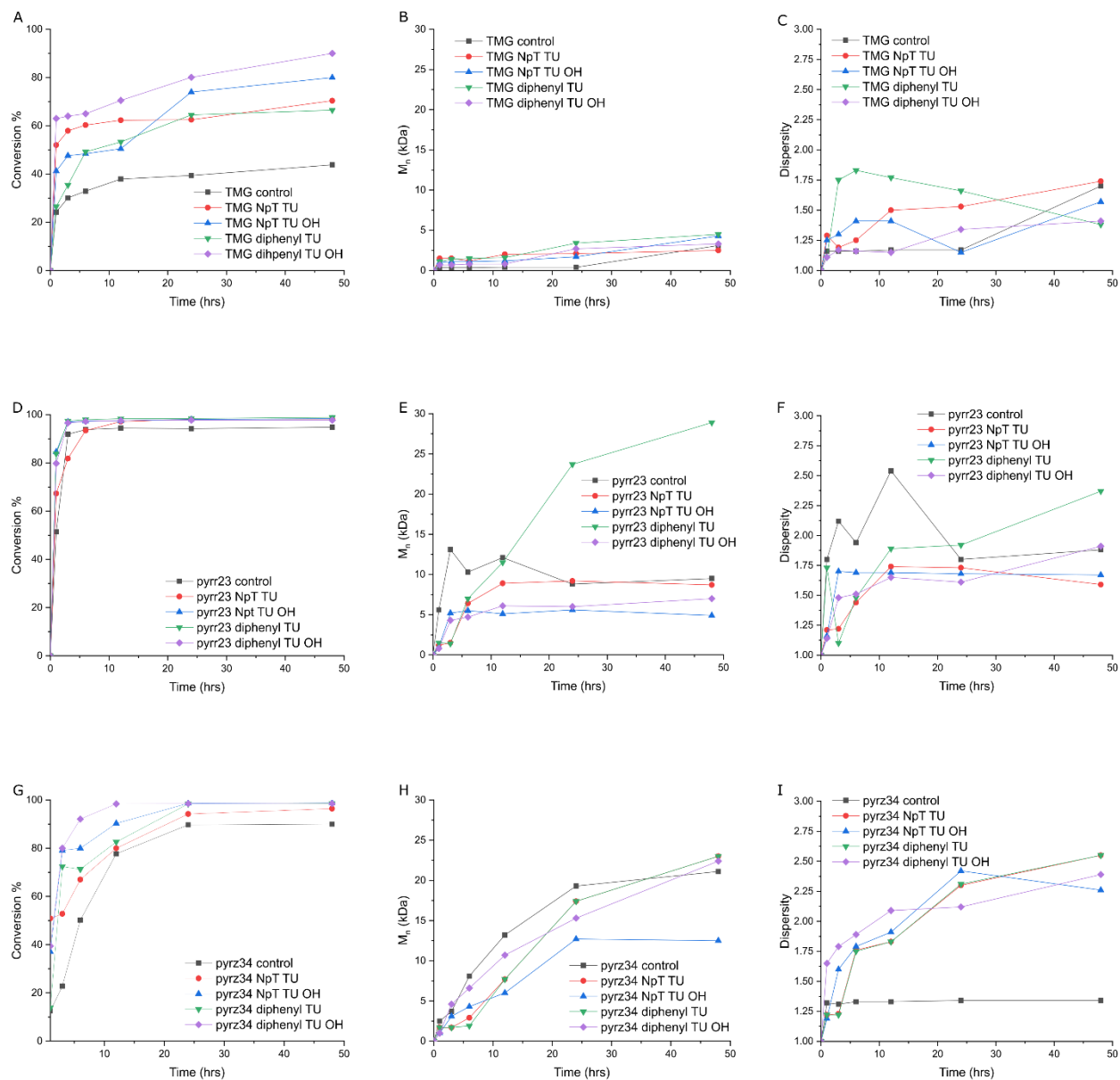
SI Figure 1: SEC traces of poly(CHA-co-AGE) catalyzed by the TMG catalyst with cocatalysts Npt TU (A), and diphenyl TU (B) and the initiator prop OH (C,D).



SI Figure 2: SEC traces of poly(CHA-co-AGE) catalyzed by the pyr23 catalyst with cocatalysts Npt TU (A), and diphenyl TU (B), and the initiator prop OH (C,D).



SI Figure 3: SEC traces of poly(CHA-co-AGE) catalyzed by the pyr34 catalyst with cocatalysts Npt TU (A), and diphenyl TU (B) and the initiator prop OH (C,D).



**SI Figure 4: Kinetic plots of conversion vs. time,  $M_n$  (kDa) vs. time, and dispersity vs. time for TMG (A, B, C), pyr23 (D, E, F), and pyr34 (G, H, I) catalytic systems.**



**SI Table 1: TMG catalyzed polymerization results**

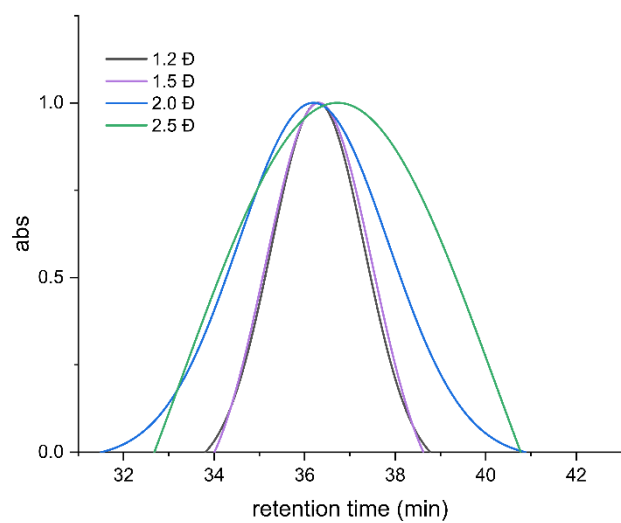
Catalyst/cocatalyst	Time (h)	M <sub>n</sub> (NMR) (kDa)	M <sub>n</sub> (SEC) (kDa)	TOF (h <sup>-1</sup> )	Conversion %	Ester linkage	Dispersity (Đ) (M <sub>w</sub> /M <sub>n</sub> )
TMG	1	0.7	0.3	48.4	24.2	84	1.16
	3	0.7	0.3	20.1	60.2	99	1.16
	6	0.8	0.3	11.0	65.8	99	1.16
	12	0.8	0.3	6.3	75.8	90	1.17
	24	1.1	0.3	3.3	78.8	96	1.17
	48	2.4	1.9	1.8	87.6	95	1.70
TMG/Npt TU	1	1.1	1.2	125.0	62.5	93	1.29
	3	1.4	1.2	46.9	70.4	95	1.19
	6	1.5	1.2	20.7	62.3	94	1.25
	12	1.6	1.4	10.1	60.3	99	1.50
	24	1.5	1.4	4.8	57.9	98	1.53
	48	2.0	1.5	2.2	52.0	94	1.74
TMG/Npt TU w prop OH	1	1.0	0.8	48.4	12.2	89	1.25
	3	1.1	0.8	19.9	29.2	97	1.30
	6	1.1	0.8	9.7	30.0	97	1.41
	12	1.2	0.8	5.6	33.5	96	1.41
	24	1.7	1.5	5.7	68.1	96	1.15
	48	4.3	3.0	2.9	68.6	95	1.57
TMG/diphenyl TU	1	1.5	0.9	113.8	56.9	97	1.11
	3	1.5	0.8	30.3	45.5	95	1.75
	6	1.2	1.0	10.3	60.8	97	1.83
	12	2.0	0.8	10.0	60.0	98	1.77
	24	2.1	3.3	5.7	68.8	99	1.16
	48	2.5	3.7	2.9	69.0	94	1.38
TMG/diphenyl TU w prop OH	1	0.3	0.6	118.4	59.2	99	1.11
	3	0.3	0.5	40.5	60.8	97	1.17
	6	0.3	0.6	17.2	51.5	98	1.16
	12	0.4	0.6	8.7	52.0	95	1.15
	24	2.4	1.9	5.9	70.5	97	1.34
	48	3.1	2.5	3.6	85.7	96	1.41

**SI Table 2: Pyrr23 catalyzed polymerization results**

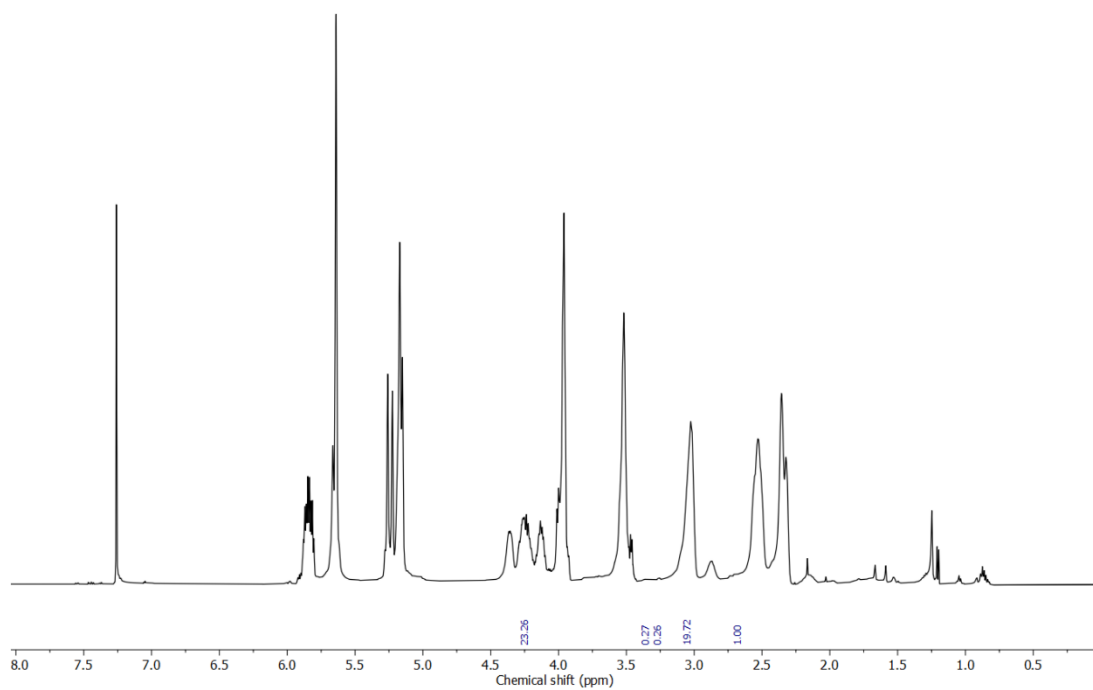
Catalyst/cocatalyst	Time (h)	M <sub>n</sub> (NMR) (kDa)	M <sub>n</sub> (SEC) (kDa)	TOF (h <sup>-1</sup> )	Conversion %	Ester linkage	Dispersity (Đ) (M <sub>w</sub> /M <sub>n</sub> )
Pyrr23	1	3.5	5.6	102.8	51.4	99	1.80
	3	12.0	13.1	61.3	91.9	99	2.12
	6	11.7	10.3	31.3	93.8	95	1.94
	12	12.9	12.1	15.7	94.4	97	2.54
	24	9.4	8.8	7.9	94.2	98	1.80
	48	9.3	9.5	4.0	94.8	98	1.88
Pyrr23/Npt TU	1	0.6	1.0	134.6	67.3	98	1.21
	3	0.8	1.2	54.5	81.8	97	1.22
	6	3.2	5.2	31.3	93.4	98	1.44
	12	4.5	5.9	16.2	97.1	98	1.74
	24	4.6	6.2	8.2	98.1	97	1.73
	48	4.4	6.4	4.1	98.2	98	1.59
Pyrr23/Npt TU w prop OH	1	0.5	0.8	158.2	79.1	99	1.16
	3	2.6	3.1	60.0	90.0	97	1.70
	6	2.8	2.9	30.6	91.8	97	1.69
	12	2.6	3.4	15.7	94.0	98	1.69
	24	2.8	2.9	7.9	95.0	97	1.68
	48	2.4	3.2	3.9	93.6	96	1.67
Pyrr23/diphenyl TU	1	0.8	1.5	158.2	79.7	99	1.73
	3	3.5	1.4	60.7	90.0	96	1.10
	6	8.0	7.0	31.3	91.8	96	1.48
	12	11.9	11.5	15.8	94.0	97	1.89
	24	14.5	23.7	7.9	95.0	97	1.92
	48	18.6	28.9	4.0	93.6	96	2.37
Pyrr23/diphenyl TU w prop OH	1	0.4	0.5	152.6	76.3	98	1.14
	3	2.2	2.9	58.7	88.0	98	1.48
	6	2.4	2.9	31.2	93.5	96	1.51
	12	3.0	2.8	15.9	95.3	94	1.65
	24	3.0	3.2	7.9	95.7	97	1.61
	48	3.5	3.2	4.1	97.4	97	1.91

**SI Table 3: Pyr34 catalyzed polymerization results**

Catalyst/cocatalyst	Time (h)	M <sub>n</sub> (NMR) (kDa)	M <sub>n</sub> (SEC) (kDa)	TOF (h <sup>-1</sup> )	Conversion %	Ester linkage	Dispersity (Đ) (M <sub>w</sub> /M <sub>n</sub> )
Pyr34	1	1.3	2.0	25.0	12.5	98	1.32
	3	3.1	3.1	15.2	22.8	95	1.31
	6	6.1	7.1	16.4	50.2	95	1.33
	12	11.7	12.0	13.0	78.0	95	1.33
	24	13.04	17.7	7.4	89.7	99	1.34
	48	17.8	19.3	3.8	90.0	99	1.34
Pyr34/Npt TU	1	1.4	1.7	101.8	50.9	91	1.31
	3	1.4	1.7	105.6	52.8	96	1.21
	6	1.7	2.9	22.3	67.0	98	1.76
	12	6.4	7.7	13.3	80.0	99	1.83
	24	16.4	17.4	7.9	94.2	97	2.30
	48	26.9	23.0	4.0	96.4	97	2.55
Pyr34/Npt TU w prop OH	1	0.5	0.8	101.8	12.5	96	1.19
	3	1.6	2.1	35.2	22.8	96	1.60
	6	2.2	2.6	22.3	50.2	97	1.79
	12	3.0	3.5	13.3	78.0	99	1.91
	24	6.4	5.7	7.9	89.7	96	2.42
	48	6.3	6.4	4.0	90.0	97	2.26
Pyr34/diphenyl TU	1	0.9	0.9	27.6	13.8	99	1.22
	3	0.9	1.3	47.5	71.3	98	1.22
	6	5.5	5.5	24.1	72.4	98	1.75
	12	8.1	7.2	13.8	82.6	98	1.83
	24	18.6	15.1	7.8	93.5	96	2.31
	48	16.6	14.8	4.0	95.2	97	2.55
Pyr34/diphenyl TU w prop OH	1	0.5	0.4	27.6	41.8	97	1.65
	3	2.3	2.6	47.5	74.4	93	1.79
	6	3.3	3.3	24.1	87.7	97	1.89
	12	5.4	3.8	13.8	95.2	97	2.09
	24	7.7	6.4	7.8	96.2	97	2.12
	48	9.5	6.0	3.9	96.0	96	2.39

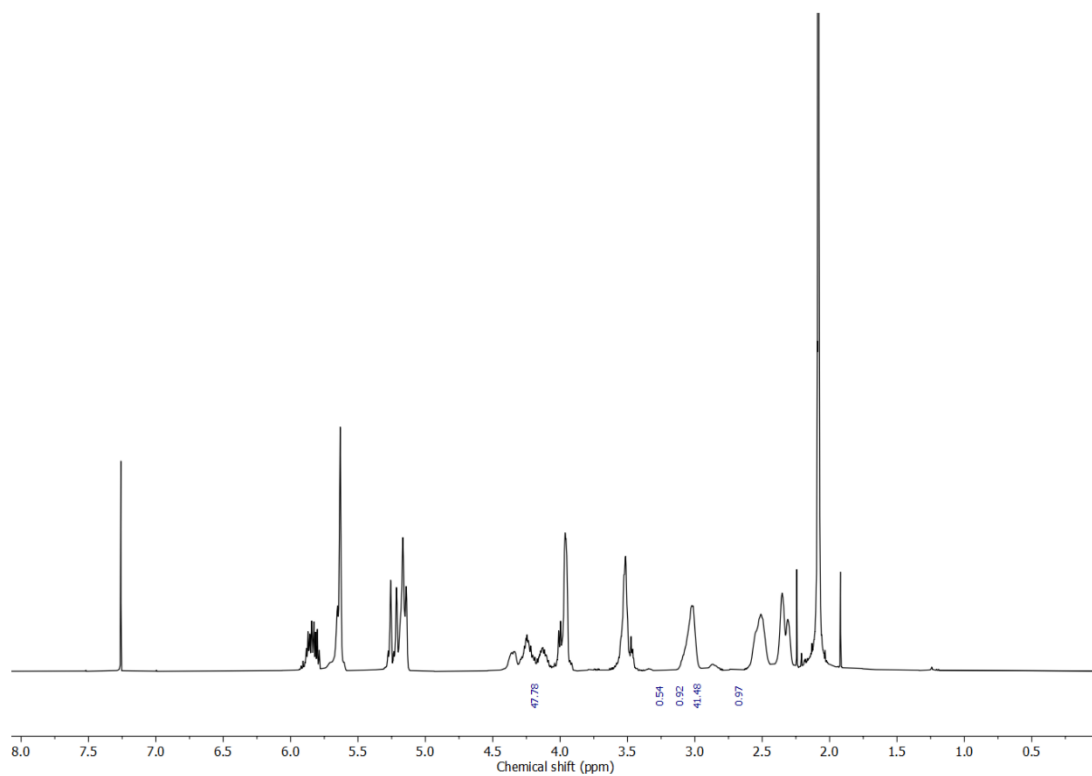


SI Figure 5: SEC traces of polyesters yielding dispersities from 1.2 Đ to 2.5 Đ used for comparisons of thermal, rheological, and mechanical properties.



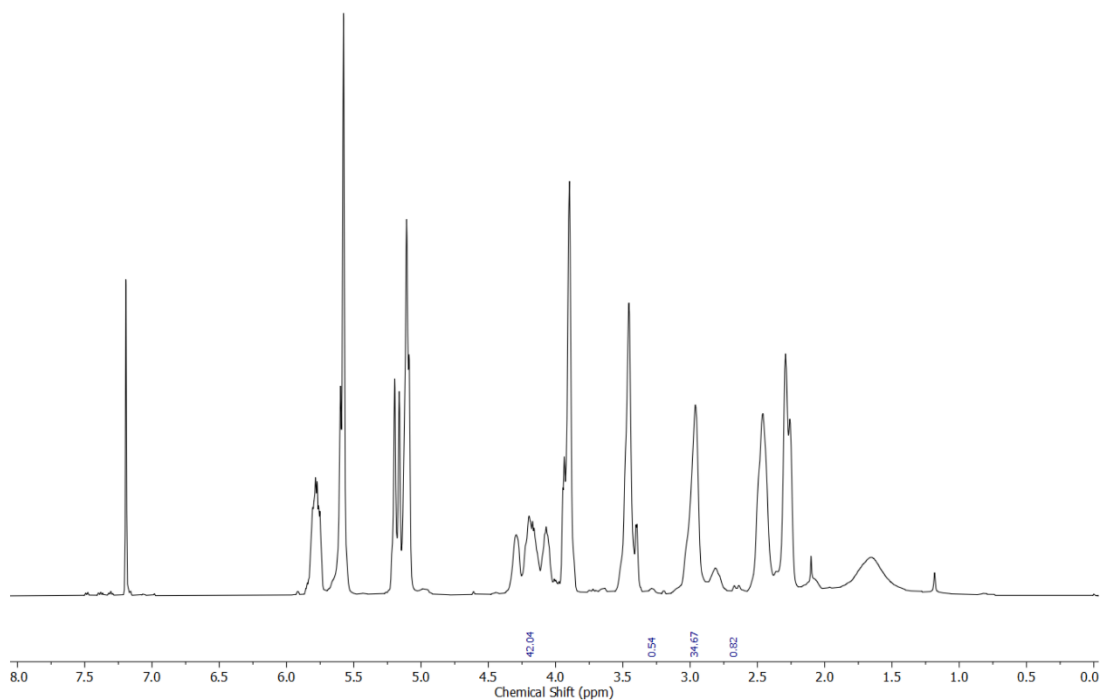
SI Figure 6: 1.2-D-CHA-co-AGE polyester  $^1\text{H}$  NMR. (500 MHz, 298 K,  $\text{CDCl}_3$ )

$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.78 (ddq,  $J = 16.5, 10.9, 4.5$  Hz, 2H), 5.59 (d,  $J = 11.6$  Hz, 3H), 5.18 (d,  $J = 17.3$  Hz, 2H), 5.10 (d,  $J = 9.8$  Hz, 3H), 4.29 (s, 1H), 4.24 – 4.02 (m, 2H), 3.95 – 3.88 (m, 3H), 3.46 (q,  $J = 8.1$  Hz, 3H), 3.05 – 2.93 (m, 3H), 2.81 (s, 1H), 2.52 – 2.41 (m, 3H), 2.27 (d,  $J = 18.0$  Hz, 3H).



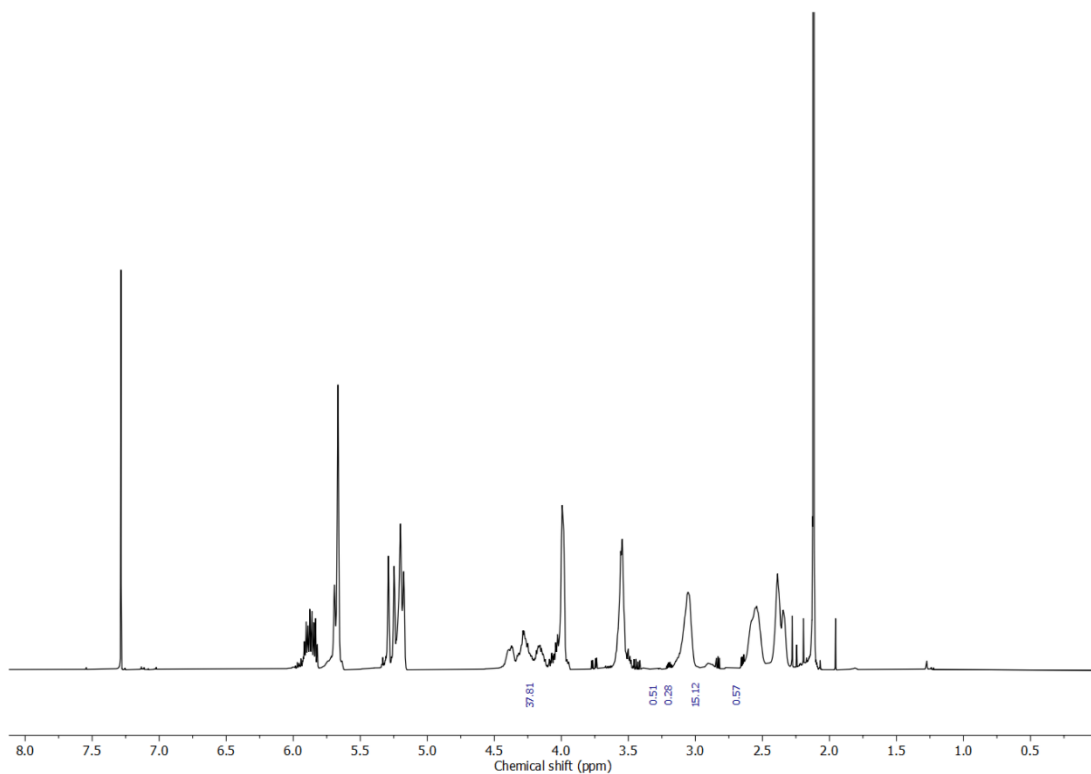
SI Figure 7: 1.5 D CHA-*co*-AGE polyester  $^1\text{H}$  NMR. (500 MHz, 298 K,  $\text{CDCl}_3$ )

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.91 – 5.77 (m, 2H), 5.64 (d,  $J = 9.2$  Hz, 4H), 5.30 – 5.12 (m, 7H), 4.31 – 4.18 (m, 1H), 4.17 – 4.06 (m, 1H), 4.04 – 3.90 (m, 5H), 3.58 – 3.43 (m, 5H), 3.02 (s, 4H), 2.86 (s, 1H), 2.51 (s, 4H), 2.31 (s, 1H).



SI Figure 8: 2.0 D CHA-co-AGE polyester  $^1\text{H}$  NMR. (500 MHz, 298 K,  $\text{CDCl}_3$ )

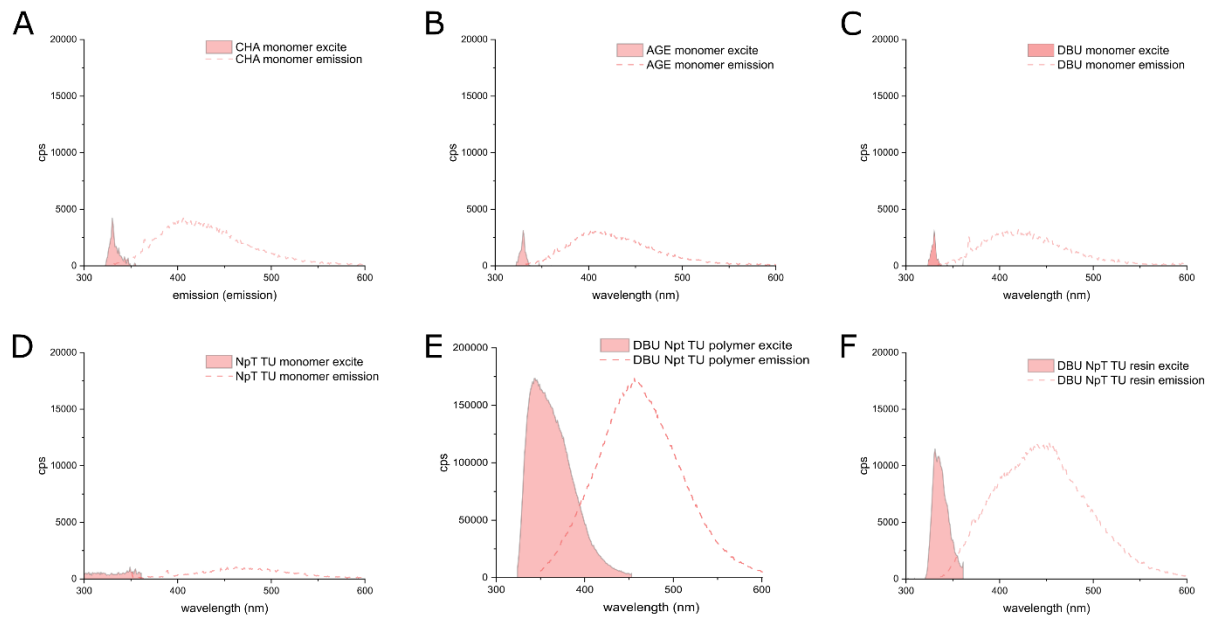
$^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  5.84 (ddt,  $J = 16.3, 10.7, 5.5$  Hz, 2H), 5.65 (d,  $J = 11.9$  Hz, 4H), 5.24 (d,  $J = 17.2$  Hz, 2H), 5.16 (d,  $J = 10.3$  Hz, 4H), 4.41 – 4.32 (m, 1H), 4.24 (ddp,  $J = 25.3, 13.1, 5.4$  Hz, 2H), 4.13 (dq,  $J = 11.8, 5.8$  Hz, 1H), 4.00 (t,  $J = 6.4$  Hz, 1H), 3.97 (s, 1H), 3.96 (s, 2H), 3.60 – 3.43 (m, 4H), 3.08 (s, 1H), 3.04 (dq,  $J = 16.5, 5.5$  Hz, 3H), 2.88 (s, 1H), 2.53 (td,  $J = 15.5, 6.2$  Hz, 4H), 2.38 – 2.29 (m, 4H).



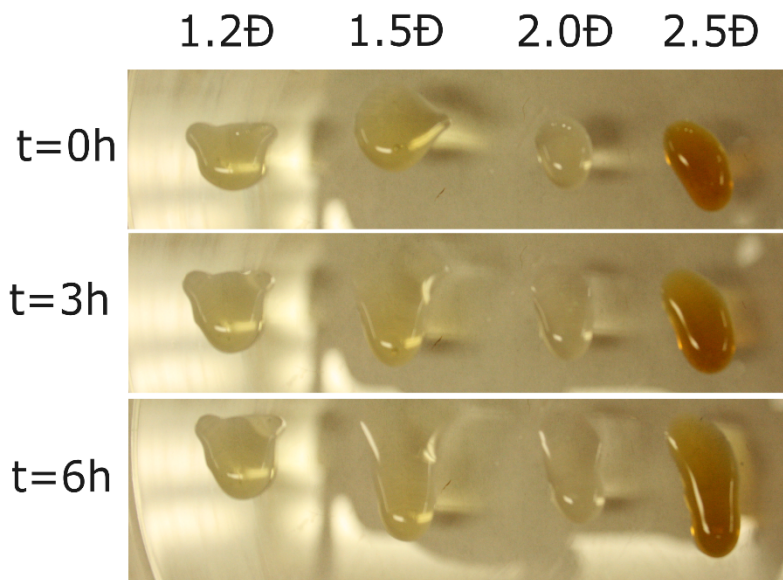
SI Figure 9: 2.5 D CHA-co-AGE polyester  $^1\text{H}$  NMR. (500 MHz, 298 K,  $\text{CDCl}_3$ )

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.94 – 5.80 (m, 1H), 5.68 (d,  $J = 10.7$  Hz, 3H), 5.34 – 5.15 (m, 4H), 4.38 (d,  $J = 9.9$  Hz, 1H), 4.28 (s, 1H), 4.07 – 3.96 (m, 3H), 3.60 – 3.46 (m, 3H), 3.06 (s, 3H), 2.55 (s, 3H), 2.33 (d,  $J = 6.9$  Hz, 1H).





SI Figure 10: Fluorescence spectra of the monomer starting materials (A-D), as well as the fluorescence of the poly(CHA-co-AGE\_ polymer (E) and resin (F) catalyzed by the DBU Npt TU system.



SI Figure 11: Visual viscosity comparison between poly(CHA-co-AGE) polymers of varying dispersity at room temperature on a 45° angle.

## References

- (1) Luo, Y.; Le Fer, G.; Dean, D.; Becker, M. L. 3D Printing of Poly(Propylene Fumarate) Oligomers: Evaluation of Resin Viscosity, Printing Characteristics and Mechanical Properties. *Biomacromolecules* **2019**, *20* (4), 1699–1708. <https://doi.org/10.1021/acs.biomac.9b00076>.
- (2) Luo, Y.; Dolder, C. K.; Walker, J. M.; Mishra, R.; Dean, D.; Becker, M. L. Synthesis and Biological Evaluation of Well-Defined Poly(Propylene Fumarate) Oligomers and Their Use in 3D Printed Scaffolds. *Biomacromolecules* **2016**, *17* (2), 690–697. <https://doi.org/10.1021/acs.biomac.6b00014>.
- (3) Abel, B. A.; Lidston, C. A. L.; Coates, G. W. Mechanism-Inspired Design of Bifunctional Catalysts for the Alternating Ring-Opening Copolymerization of Epoxides and Cyclic Anhydrides. *J. Am. Chem. Soc.* **2019**, *141* (32), 12760–12769. <https://doi.org/10.1021/jacs.9b05570>.
- (4) DiCiccio, A. M.; Coates, G. W. Ring-Opening Copolymerization of Maleic Anhydride with Epoxides: A Chain-Growth Approach to Unsaturated Polyesters. *J. Am. Chem. Soc.* **2011**, *133* (28), 10724–10727. <https://doi.org/10.1021/ja203520p>.
- (5) Fieser, M. E.; Sanford, M. J.; Mitchell, L. A.; Dunbar, C. R.; Mandal, M.; Van Zee, N. J.; Urness, D. M.; Cramer, C. J.; Coates, G. W.; Tolman, W. B. Mechanistic Insights into the Alternating Copolymerization of Epoxides and Cyclic Anhydrides Using a (Salph)AlCl and Iminium Salt Catalytic System. *J. Am. Chem. Soc.* **2017**, *139* (42), 15222–15231. <https://doi.org/10.1021/jacs.7b09079>.
- (6) Xu, J.; Chen, Y.; Xiao, W.; Zhang, J.; Bu, M.; Zhang, X.; Lei, C. Studying the Ring-Opening Polymerization of 1,5-Dioxepan-2-One with Organocatalysts. *Polymers* **2019**, *11* (10), 1642. <https://doi.org/10.3390/polym11101642>.
- (7) Merckle, D.; Constant, E.; Cartwright, Z.; Weems, A. C. Ring Opening Copolymerization of Four-Dimensional Printed Shape Memory Polyester Photopolymers Using Digital Light Processing. *Macromolecules* **2021**, *54* (6), 2681–2690. <https://doi.org/10.1021/acs.macromol.0c02401>.
- (8) Merckle, D.; King, O.; Weems, A. C. Ring-Opening Copolymerization of Four-Dimensional Printable Polyesters Using Supramolecular Thiourea/Organocatalysis. *ACS Sustain. Chem. Eng.* **2023**, *11* (6), 2219–2228. <https://doi.org/10.1021/acssuschemeng.2c05552>.