

# Toughness Enhancers for Bone Scaffold Materials Based on Biocompatible Photopolymers

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**ABSTRACT:** Providing access to the benefits of additive manufacturing technologies in tissue engineering, vinyl esters recently came into view as appropriate replacements for (meth)acrylates as precursors for photopolymers. Their low cytotoxicity and good biocompatibility as well as favorable degradation behavior are their main assets. Suffering from rather poor mechanical properties, particularly in terms of toughness, several improvements have been made over the last years. Especially, thiol–ene chemistry has been investigated to overcome those shortcomings. In this study, we focused on additional means to further improve the toughness of an already established biocompatible vinyl ester–thiol formulation, eligible for digital

light processing-based stereolithography. All molecules were based on poly( $\epsilon$ -caprolactone) as building block and the formulations were tested regarding their reactivity and the resulting mechanical properties. They all performed well as toughness enhancer, ultimately doubling the impact resistance of the reference system. © 2018 The Authors. *Journal of Polymer Science Part A: Polymer Chemistry* published by Wiley Periodicals, Inc. *J. Polym. Sci., Part A: Polym. Chem.* **2018**

**KEYWORDS:** biomaterials; FT-IR; monomers; photopolymerization; polyesters; rheology

**INTRODUCTION** Additive manufacturing technologies (AMTs) have already made their entrance in biomedical engineering over the past few decades, facilitating the fabrication of medical devices, surgical guides and most recently patient specific implants for regenerative therapy.<sup>1–3</sup> The latter especially benefits from lithography-based AMTs (L-AMTs), where photosensitive resins are employed to produce structures with high feature resolution and complex geometry. This enables the fabrication of scaffolds for tissue engineering according to the replaced structure in the biological system.<sup>4</sup> In case of bone tissue engineering, this includes porosity, ranging from the highly dense outer bone layer (*compacta*) to the highly porous, marrow-containing center of the bone (*spongiosa*) along with over all considerably complex patient-specific geometries.<sup>5,6</sup> The opportunity to target malfunctions and diseases of various tissues and organs, claims further research on appropriate materials and optimization of fabrication methods.<sup>7,8</sup> A broad range of benchmarks has to be met to fully exploit L-AMTs for medical purposes. A common obstacle

for scaffolds in tissue engineering is suitable mechanical properties for different applications (e.g., replacement materials for bone, cardiovascular system, cartilage, etc.). In order to provide good load dissipation and tissue integration, mechanical properties like tensile strength and Young's modulus of the scaffold have to match those of the replaced tissue. In case of photopolymers, especially sufficient toughness is an issue that needs to be targeted, as highly crosslinked networks behave very brittle.

Current state-of-the-art monomers for digital light processing–stereolithography (DLP–SLA) are (meth)acrylates, combining favorable reactivity and mechanical properties.<sup>6,9</sup> Especially, methacrylates can also be found as prominent examples for currently applied materials used in treatment of bone injuries (as bone cement) and in dental restoratives.<sup>5</sup> Nevertheless, the applicability in this field is still limited due to the cytotoxicity of (meth)acrylates and their unfavorable degradation products (polyacids).<sup>10,11</sup>

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Vinyl esters (VEs) emerged as promising alternatives, showing favorable reactivity along with low cytotoxicity.<sup>10–13</sup> However, homopolymers of, for example, divinyl adipate (DVA, the only multifunctional commercially available VE) are very brittle and frequently break during crosslinking owing to the high shrinkage stress. A well explored way to modify such brittle photopolymer networks is the employment of chain-transfer agents (CTAs), for example, thiols. The resulting networks exhibit lower shrinkage stress and higher fracture toughness. This is often accompanied by a decreased modulus and a sharpened glass transition temperature.<sup>13</sup> In case of VE, thiol-ene chemistry comes along with increased reactivity, as the intermolecular H-abstraction is suppressed as well as lower susceptibility toward oxygen inhibition is achieved.<sup>13,14</sup> Besides their good biocompatibility, these polymers show little to no signs of autocatalytic bulk erosion, rather following a favorable surface erosion mechanism with biocompatible degradation products (poly[vinyl alcohol]).<sup>10,12</sup>

Formulation based on DVA were successfully fabricated into scaffolds using L-AMT and subjected to *in vivo* testing.<sup>15</sup> However, the obtained structures lacked sufficient toughness for bone graft substitutes (especially for screwed implants) and required further improvement, which is topic of the present study.

In addition to thiol-ene chemistry, there are several other methods known in literature to improve toughness in photopolymer networks, most of them derived from techniques used for epoxy resins.<sup>11,16–19</sup> A very versatile approach is based on blending with high-molecular-weight substances. Even just by physical interactions, this results in reduced network density and enables additional means to dissipate employed stress. The effect can be further improved by introducing chemical crosslinking. Another approach is the incorporation of urethane functionalities, also known as efficient method to increase toughness.<sup>11,20</sup> Biomaterials containing polyurethanes are widely used as dental restoratives and are in consideration for vascular grafts and heart valves for reasons of their high durability, toughness, and biocompatibility.<sup>21–23</sup>

The aim of this study was to design and prepare molecules and oligomers with the capability to further improve the toughness of an established photopolymerizable vinyl ester-based thiol-ene network already investigated for the fabrication of bone graft substitutes by DLP-SLA.<sup>13</sup> The term “additive” was used to refer to those substances; although in some cases, the interactions with the formulation to be enhanced were not only physically. The formulation referred to as “reference” consisted of commercially available DVA, mixed with the 3-arm thiol trimethylolpropane tris(3-mercaptopropionate) (TMPMP).<sup>24</sup> The resulting thiol-ene network already exhibited great improvements regarding reactivity, double bond conversion (DBC) and mechanical properties due to a more regulated and less dense network architecture compared to homopolymerized DVA.<sup>11,13</sup> A rather simple way to further improve toughness is blending the photopolymerizable resin with a high-molecular-weight, linear polymer. For this purpose, Capa 6250 (poly( $\epsilon$ -caprolactone) [PCL]), a commercially available with a molecular weight of 25 kg mol<sup>-1</sup>,

was selected. Thermoplasts based on PCL are well established in biomedical applications, their main assets being good biocompatibility and biodegradability.<sup>25</sup> Physical interactions and sterical restrictions generally lead to a decrease in crosslink density through the addition of PCL.<sup>26</sup> A more sophisticated approach included the functionalization of the same linear polymer with copolymerizable end groups, enabling a chemical interaction with the thiol-ene network. Opening up further modification possibilities, a high-molecular-weight urethane dithiol (UDT) containing rigid cyclic structures was synthesized and used as additional CTA. The resulting resin formulations were expected to exhibit high reactivity and result in low toxic, tough, biocompatible and degradable polymer networks. The impact of various concentrations of additives was investigated in means of chemical (reactivity, DBC, gel point) and (thermo-)mechanical behavior (modulus, tensile strength, elongation at break, impact resistance, glass transition temperature).

## EXPERIMENTAL

### Materials

All chemicals were used as received if not stated otherwise. Divinyl adipate (DVA) was purchased from TCI Europe (Zwijndrecht, Belgium), 3,6-dioxa-1,8-octane dithiol (DOD), vinyl chloroformate, trimethylamine, HCl (37% aqueous solution), and triethylamine (Et<sub>3</sub>N) were purchased from Sigma-Aldrich (St. Louise, MO). Anhydrous Na<sub>2</sub>SO<sub>4</sub> was purchased from VWR International GmbH (Vienna, Austria). TMPMP was kindly donated by Bruno Bock Chemische Fabrik GmbH & Co KG, Marschacht, Germany. Capa 6250, a high-molecular-weight linear  $\alpha,\omega$ -hydroxy polyester derived from  $\epsilon$ -caprolactone with a molecular weight ( $\overline{M}_n$ ) of 25 kg mol<sup>-1</sup> (stated on the data sheet and confirmed by hydroxyl end-group titration), was received from Perstorp AB (Malmö, Sweden). Genomer 4215 (UDA), an aliphatic polyester urethane diacrylate was received from Rahn AG (Zurich, Switzerland). The molecular weight on the data sheet was stated to be 1.5 kg mol<sup>-1</sup>, which was confirmed by gel permeation chromatography (GPC) and nuclear magnetic resonance (NMR).<sup>27</sup> Dichloromethane and other solvents were distilled and stored over molecular sieve prior to use. The used photoinitiator (PI) 1,1'-(diethylgermylene)bis[1-phenylmethanone] (Ivocerin) was kindly supplied by Ivoclar Vivadent (Schaan, Lichtenstein).

### Characterization

<sup>1</sup>H NMR spectra were recorded on a Bruker Avance 400 MHz Fourier transform-NMR spectrometer, using CDCl<sub>3</sub> as a solvent (grade of deuteration of at least 99.5%). The signal of CHCl<sub>3</sub> at 7.26 ppm was used as reference for calibration. Attenuated total reflection-Fourier transform infrared (ATR-FTIR) measurements were conducted on a Biorad FTS 135 spectrophotometer with a Golden Gate MkII diamond ATR equipment. GPC measurements were performed on a Malvern VISCOTEK TDA system with a VISCOTEK SEC-MALS 9 light scattering detector. Samples were separated through three consecutive Polymer Standards Service (PSS, Mainz, Germany) styrene-divinylbenzene copolymer network (SDC) columns using tetrahydrofuran (THF) as solvent. Universal calibration was done using triple

detection. Degree of functionalization with double bonds (DS) of divinyl carbonate (DVC) modified PCL was determined by titration of iodine value (IoV) using the Wijs Method.<sup>28</sup>

## Synthesis Procedures

### Synthesis of DVC Modified PCL

Capa 6250 (6.25 g, 1 eq., 0.25 mmol) and dry pyridine (0.1 mL, 4 eq., 1 mmol) were dissolved in 66 mL of dry dichloromethane under argon atmosphere and cooled to 0 °C. Vinyl chloroformate (0.1 mL, 4 eq., 1 mmol) was added dropwise to the stirred solution within 10 min. The reaction was kept at 0 °C for 30 min and stirred for another period of 2 h at room temperature. The mixture was diluted with 50 mL dichloromethane and extracted twice with 50 mL 1 N HCl. The organic phase was dried with anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was removed under vacuum. The crude product was dissolved in THF and precipitated in petrol ether to give 6.0 g (96%th) DVC as a white solid. <sup>1</sup>H NMR (400 MHz, CHCl<sub>3</sub>): (δ ppm) = 7.07 (dd, 2H, J<sub>1</sub> = 13.9 Hz, J<sub>2</sub> = 6.2 Hz, CH<sub>2</sub>-CH-O-), 4.90 (dd, 2H, J<sub>1</sub> = 13.8 Hz, J<sub>2</sub> = 2.0 Hz, CH<sub>2</sub>-CH-O- *trans*), 4.56 (dd, 2H, J<sub>1</sub> = 6.2 Hz, J<sub>2</sub> = 2.1 Hz, CH<sub>2</sub>-CH-O- *cis*), 4.19 (t, 4H, J = 6.4 Hz, -O-CH<sub>2</sub>-CH<sub>2</sub>-O-), 4.05 (t, ~400H, J = 6.7 Hz, -CO-O-CH<sub>2</sub>-CH<sub>2</sub>-), 2.30 (t, ~400H, J = 7.59 Hz, -O-CO-CH<sub>2</sub>-CH<sub>2</sub>-), 1.68–1.33 (m, ~1300H, -CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-CH<sub>2</sub>-), DS calculated from IoV = 99.8 ± 3.7%, GPC (THF):  $\overline{M}_n$  = 24 kg mol<sup>-1</sup>.

### Synthesis of UDT

Genomer 4215 (15.00 g, 2 eq., 10 mmol) was dissolved in 150 mL THF under argon atmosphere and DOD (2.73 g, 3 eq., 15 mmol) was added in one shot.<sup>29</sup> Under vigorous stirring triethylamine (1.8 mL, 13 mmol) was added. The reaction was stirred for 8 days at room temperature with daily determination of residual double bonds by ATR-FTIR. As soon as no double bonds were detectable, the reaction mixture was poured on a large excess of cold petroleum ether and the product precipitated as viscous, white substance. The supernatant was filtered through a suction flask with a sintered glass filter and afterward discarded. The precipitate was dissolved in dichloromethane, filtered, and the solvent was removed again in vacuum to obtain 17.1 g (97%th) UDT as a highly viscous, slightly yellowish liquid. <sup>1</sup>H NMR (400 MHz, CHCl<sub>3</sub>): (δ ppm) = 4.91–4.51 (m, 8H, -NH-), 4.23 (m, 24H, -NH-CO-O-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-O-), 4.05 (m, 24H, -CO-O-CH<sub>2</sub>-), 3.74–3.61 (m, 34H, CH=CH-CO-O-CH<sub>2</sub>-S-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-), 3.38 (s, 4H, NH-CH<sub>2</sub>-), 2.90–2.63 (m, 20H, S-CH<sub>2</sub>-CH<sub>2</sub>-O-), 2.36–2.28 (m, 24H, -CO-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-), 1.97–1.37 (m, ~130H, -CH<sub>2</sub>-), 1.09 (m, 36H, IPDI -CH<sub>3</sub>); IR (ATR):  $\nu$  (cm<sup>-1</sup>) 3344, 2928, 2858, 1725, 1522, 1451, 1415, 1350, 1226, 1162, 1098, 1063, 978, 901, 809, 776, 736; GPC (THF):  $\overline{M}_n$  = 3.5 kg mol<sup>-1</sup>.

## Preparation of Resin Formulations

All resin formulations were freshly prepared and stored in the dark before measurement or casting due to limited storage stability of the UDT containing formulations (<1 week). Every formulation contained 0.5 wt % Ivocerin as PI. Furthermore, 0.02 wt % pyrogallol were added to circumvent the problem of low storage stability of thiol-ene formulations and ensure

sufficient stability of the formulations.<sup>30,31</sup> The PI and stabilizer were added after the addition of the respective additive. Due to solubility and viscosity, samples containing additives were stored at 60 °C until processing. The formulations were then mixed with a vortex mixer and degassed in an ultrasonic bath for approximately 20 min. All formulations are labeled with the code XXX\_YY, where XXX stands for the additive (PCL, DVC, or UDT) and YY for the ratio in wt %, for example, PCL<sub>15</sub> contains 15 wt % of the PCL additive. All mixtures contained a constant amount of 0.15 mol thiol groups per mol reactive double bond, 15 double bond% (db%). When the thiol-terminated UDT is added, the amount of TMPMP is reduced to maintain this ratio. The abbreviations and corresponding amounts of additives are listed in Figure 1.

## Real-Time Near-Infrared Photorheology

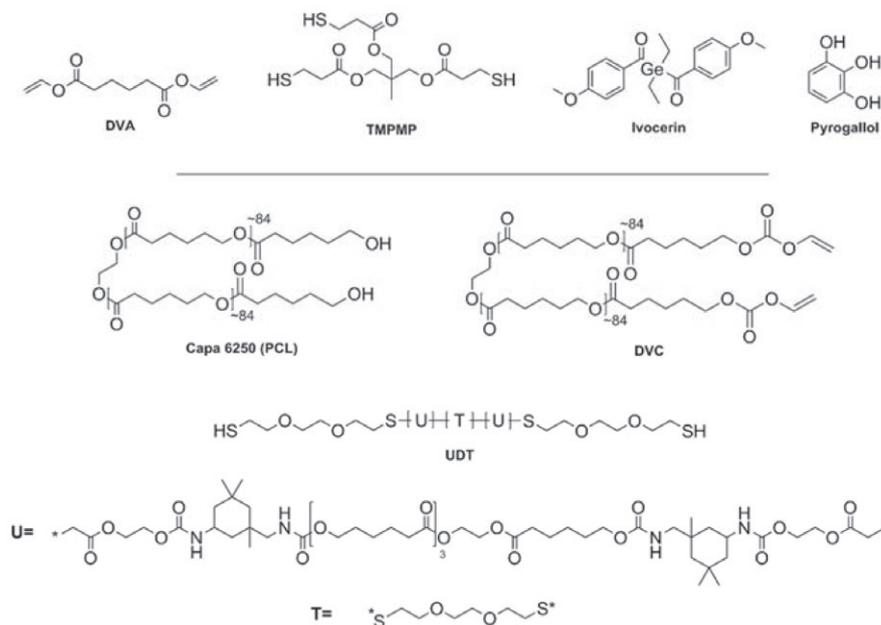
Real-time near-infrared (RT-NIR) photorheology was performed using an Anton Paar MCR302 WESP rheometer with a P-PTD 200/GL Peltier glass plate and a PP25 measuring system, coupled with a Bruker VERTEX 80 FTIR spectrometer.<sup>32</sup> The specific amount of formulation needed to fill the fixed 100 μm gap was determined empirically (63 μL). An oscillatory shear was applied to the sample with an angular strain of 1% and a frequency of 1 Hz. After an equilibration period of 60 s, the light-emitting diode (LED) light source (300 s, 460 nm, intensity at curing position 19 mW cm<sup>-2</sup>) was switched on, irradiating the sample on the glass plate and causing it to crosslink. Throughout the measurement, a NIR beam was directed through the glass plate and the sample and was reflected by the metal plate of the measuring system into an external mercury cadmium telluride (MCT) detector.

Changes in mechanical data—namely, storage and loss modulus, along with the occurring normal force—were recorded during the polymerization, at a frequency of 4 Hz. Furthermore, the gel point—which is marked by the crossing of storage ( $G'$ ) and loss modulus ( $G''$ ) curve—could be obtained ( $G''/G' = 1$ ). NIR spectra were measured at wave numbers from 4000 to 7000 cm<sup>-1</sup> with a resolution of 8 cm<sup>-1</sup> at the same acquisition frequency. A set of spectra was recorded 5 s before irradiation and averaged to serve as starting value. For the end value, the average of the last 50 measuring points—that equals a time span of 13 s—was taken. Over the acquisition time (more than 1000 individual spectra per experiment, examples at different irradiation times and conversions, respectively, can be found in the Supporting Information, Fig. S1), the respective double bond signal at ~6190 cm<sup>-1</sup> was integrated and the ratio between start and end value was used to calculate the DBC. In addition, the DBC at the gel point (DBC<sub>g</sub>) and the time to reach 95% of overall conversion ( $t_{95}$ ) were determined. All measurements were conducted at 20 °C and at least in triplicates and results are given as mean values with standard deviation (SD). Exemplary curves can be found in the Supporting Information (Fig. S2).

## Mechanical Testing

### Sample Preparation

Specimens for mechanical testing were prepared by photopolymerization of the formulations in silicone molds of



Formulation	Components	Additive (mol %) <sup>a</sup>	Additive (wt %) <sup>a</sup>	Viscosity (mPa s)
Ref	DVA + TMPMP	0.00	0	n.d. <sup>b</sup>
PCL_5	DVA + TMPMP + PCL	0.04	5	70
PCL_10	DVA + TMPMP + PCL	0.08	10	120
PCL_15	DVA + TMPMP + PCL	0.12	15	220
DVC_5	DVA + TMPMP + DVC	0.04	5	70
DVC_10	DVA + TMPMP + DVC	0.08	10	150
DVC_15	DVA + TMPMP + DVC	0.12	15	170
UDT_13	DVA + TMPMP + UDT <sup>c</sup>	1.00	13	90
UDT_31	DVA + TMPMP + UDT <sup>c</sup>	3.00	31	980
UDT_43	DVA + TMPMP + UDT <sup>c</sup>	5.00	43	4800

<sup>a</sup> mol % and wt % were calculated according to the amount of monomer DVA in the formulation.

<sup>b</sup> not determined.

<sup>c</sup> thiol to ene ratio was kept constant at 15 db %.

**FIGURE 1** Structures of the components used in the reference formulation and the investigated additives (top) and compositions and viscosities of the formulations; DVA as base monomer, TMPMP as network modifier, Ivocerin as PI, pyrogallol as stabilizer, Capa 6250 (PCL), DVC modified PCL (DVC), and UDT as additives (bottom).

respective size and shape. Photopolymerization was carried out in two steps—a primary curing with a 460 nm LED (LX500 Spot Curing System Lumen Dynamics, intensity at curing position  $44 \text{ mW cm}^{-2}$ , distance from light source 75 mm) and an exposure time of 60 s on both sides—and a postcuring step in a ventilated ultraviolet (UV) chamber (Uvitron UV 1080 Flood Curing System with Uvitron IntelliRay 600 halide lamps, irradiation power 600 W, UV-visible :  $125 \text{ mW cm}^{-2}$ , distance from light source 130 mm, intensity at curing position:  $120 \text{ mW cm}^{-2}$ ) with an exposure time of 300 s on both sides of the specimen to match the irradiation setup with the DLP-SLA machine planned to be used, as well as the required postcuring. Due to high viscosity of some formulation and addressing the problem of bubbles in the specimens, the first step of the polymerization was carried out at  $60^\circ\text{C}$ . Regarding dynamic mechanical thermal analysis (DMTA) and Dynstat Impact Test prismatic specimens (DMTA:  $2 \times 5 \times 40 \text{ mm}^3$ ,

Dynstat:  $4 \times 10 \times 15 \text{ mm}^3$ ) and for tensile testing dog-bone-shaped specimens (according ISO527-2:2012 geometry 5B with a thickness of 2 mm) were prepared. All samples were grinded and polished with sandpaper prior to the measurements to remove artifacts from the surface.

#### Dynamic Mechanical Thermal Analysis

DMTA measurements were conducted on an Anton Paar MCR 301 Rheometer with an SRF 12 measuring system and a CTD 450 oven. Tests were done in torsion mode with a frequency of 1 Hz and strain of 0.1% in a temperature range from  $-10$  to  $110^\circ\text{C}$  with a heating rate of  $2^\circ\text{C min}^{-1}$ . The specimens were initially cooled to  $-10^\circ\text{C}$  and kept isothermal for 1 min before the measurement was started. The maximum dissipation factor ( $\tan \delta$ ) was defining the glass transition temperature. Single measurements were performed.

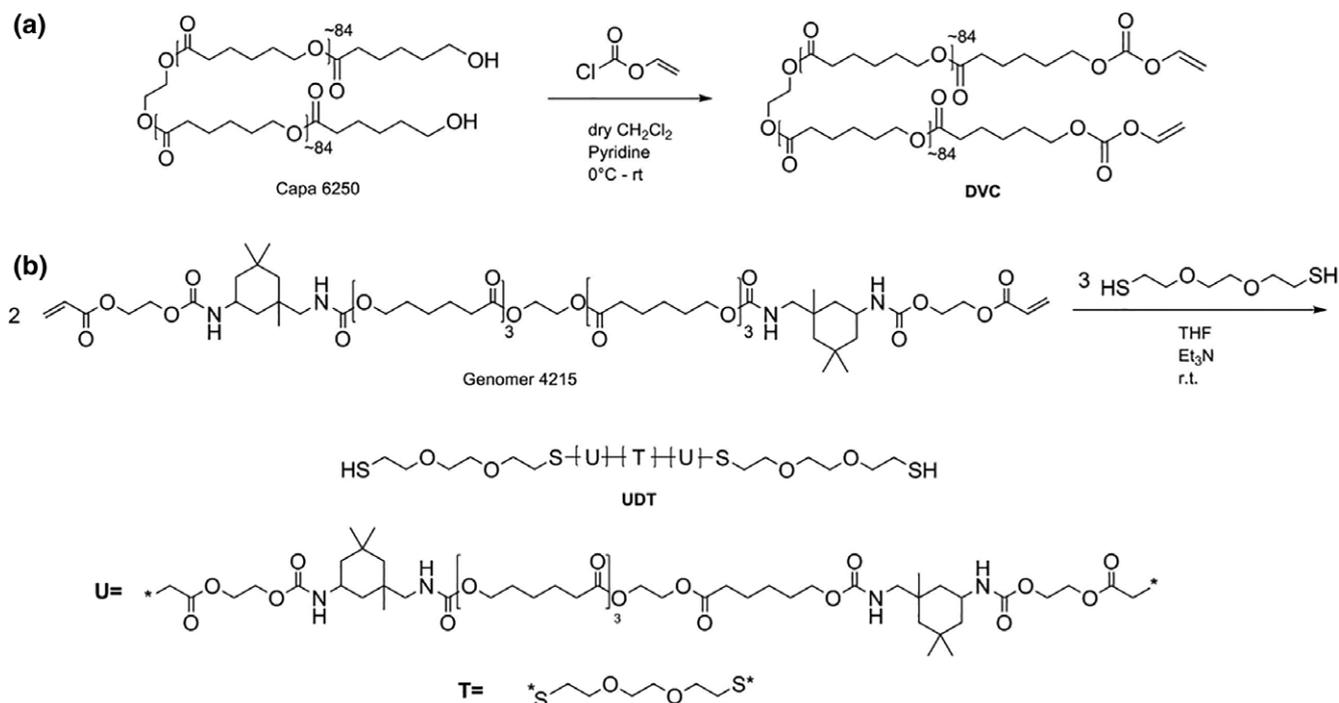


FIGURE 2 (a) Synthesis of copolymerizable DVC and (b) synthesis of UDT as novel additives for toughness enhancement.

### Dynstat Impact Resistance

Dynstat tests were performed on a Karl Frank Type 573 Dynstat machine. After the samples were fractured with a  $10 \text{ kp cm}^{-1}$  ( $0.98 \text{ N m}^{-1}$ ) hammer the values were taken from the scale, thereafter converted into  $\text{kJ}$  and divided by the cross-sectional area of the specimen in  $\text{m}^2$ . At least four specimens were tested for every formulation.

### Tensile Testing

Tensile testing was done on a Zwick Z050 tensile testing machine employing a 1 kN load sensor. The strain was measured with a mechanical extensometer, recorded and analyzed via testXpert II testing software. The crosshead speed was set for  $5 \text{ mm min}^{-1}$ . At least four specimens were tested for every formulation.

## RESULTS AND DISCUSSION

Patient specific bone graft substitutes based on additive manufactured parts have great potential in the future.<sup>3</sup> In this article, the targeted manufacturing technique is DLP-SLA, relying on photopolymerizable resins. The chosen reference system that was sought to be enhanced was selected based on previous research, since vinyl esters showed potential as suitable alternative for methacrylates in biomedical applications.<sup>13</sup> It consisted of DVA and 15 db% thiol in the form of TMPMP.

As the commercially available systems are still lacking satisfying mechanical properties, means of toughness improvement on the existing resin formulation were investigated. Different additives based on PCL were designed and

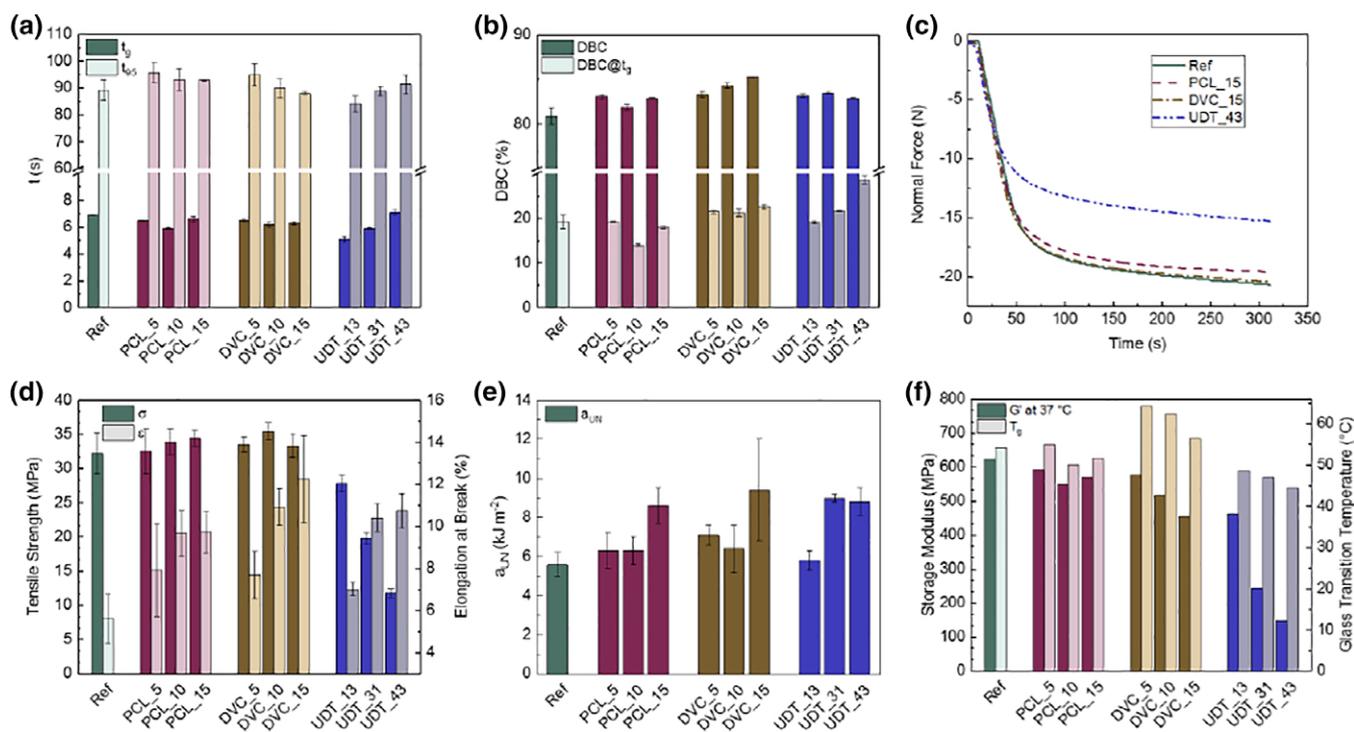
synthesized, respectively, starting from the commercially available, unreactive linear polyester Capa 6250 (hereinafter named PCL), the copolymerizable DVC modified PCL to a polyester UDT including urethane groups and cyclic structures. The structures of the molecules involved in this study can be seen in Figure 1.

### Synthesis of Additives

DVC was synthesized by converting the high-molecular-weight linear polyester diol Capa 6250 with vinyl chloroformate using pyridine as acid scavenger in nearly quantitative yields.<sup>33</sup> A thiol-Michael addition reaction was employed to synthesize UDT using triethylamine as base catalyst.<sup>29,34,35</sup> Both pathways are shown in Figure 2.

### RT-NIR Photorheology

Being able to observe changes in both chemical and mechanical behaviors during the photopolymerization reaction *in situ* by RT-NIR photorheology gave access to viable values at virtually any point of the reaction. The most important values gathered are the gel point ( $t_g$ ), the conversion at the gel point ( $\text{DBC}_g$ ), the overall DBC, the time needed to reach 95% of overall conversion ( $t_{95}$ ), and the occurring shrinkage stress, determined by the normal force ( $F_N$ ). In this context, it has to be mentioned that it was not possible to discern between double bonds originating from the vinyl ester and those from the vinyl carbonate, thus all stated DBC values represent the total conversion of all present double bonds. The  $t_g$  is the time point, where storage and loss modulus curves intersect, usually reached at rather low conversion in typical, crosslinking photopolymer networks (e.g., dimethacrylates) at about 15–20%. This



**FIGURE 3** Results of photorheological and (thermo-)mechanical analysis of formulations based on DVA containing 15 db% thiol (TMPMP) with different amounts of Capa 6250 (PCL), DVC modified PCL, or UDT as additive (the thiol content in UDT formulations was kept constant by reducing the amount of TMPMP, respectively); (a) obtained values for time to reach the gel point ( $t_g$ ) and time to reach 95% of overall conversion ( $t_{95}$ ); (b) obtained values for the overall DBC and conversion at the gel point ( $DBC_g$ ); (c) comparison of exemplary normal force curves of the reference with formulations containing the, respectively, highest amount of additive; (d) results from tensile testing including tensile strength and elongation at break; (e) results from Dynstat impact testing; and (f) results from DMTA measurements including storage modulus at 37 °C and glass transition temperature. [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

restrains chain mobility and results in high shrinkage stress as the polymerization continues in a gel-like state. Directly connected with  $t_g$  is  $DBC_g$ , which can be increased by delaying the gel point (e.g., by employing thiols as network modifier) in order to reduce shrinkage stress.<sup>36,37</sup> DBC should be as high as possible to achieve good mechanical properties.  $t_{95}$  helps characterizing the suitability of a resin for additive manufacturing. A low  $t_{95}$  is favorable for high printing speed, since the previous layer needs to be at a certain stability (i.e., conversion) to allow application of the following layer.  $F_N$  is a measure for the developed shrinkage stress and should be as low as possible.<sup>32</sup> Numerical data obtained through these measurements can be found in the Supporting Information (Table S1).

As depicted in Figure 3, the reference formulation consisting of DVA with 15 db% thiol in the form of TMPMP, reached its gel point after 6.9 s at a conversion of 19%. Throughout all additives and concentrations thereof, the gel point was hardly influenced, ranging between 5.4 and 6.9 s for the respective mixtures. The addition of the unreactive linear polyester PCL was observed to have slightly decreased  $t_g$  and  $DBC_g$ . Especially the formulation PCL<sub>10</sub> behaved out of the expected trend, as it reached the  $t_g$  fastest and with lowest conversion,

compared to the other PCL formulations. Polymerized samples containing additives based on Capa 6250 were opaque, indicating phase separation. Explanation can be given by the intricate interplay of gelation and phase separation affecting each other.<sup>38,39</sup> This is expected to increase the probability of chain propagation at lower PCL concentrations owing a prearrangement induced by the nonreacting additive.<sup>40</sup> At higher contents, the phase separation kinetics and increasing viscosity are counteracting this effect.

Addition of the high molecular weight, flexible DVC as comonomer to the rather densely crosslinking DVA resulted in a decrease in crosslink density and thus improving the mobility of the growing polymer chain in the gelling formulation. This caused a delay of gel point ( $t_g$ ) and thus the observed increase for  $DBC_g$  values.

Most interesting was the effect observed with UDT as additive, which reduced  $t_g$  to 5.6 s and  $DBC_g$  to 17% at 1 mol % (formulation UDT<sub>13</sub>) and shifted  $DBC_g$  to 24% without influencing  $t_g$  at a concentration of 5 mol % (UDT<sub>43</sub>). Usually, a lower  $t_g$  is accompanied with a decrease in  $DBC_g$  as the polymer network has less time to form prior to gelation. This also results in higher internal stress caused by the continued

reaction in this gelled state, along with an increase in polymer shrinkage. An increase in  $DBC_g$ , while reaching  $t_g$  in the same time span as the reference formulation (in case of UDT\_43) was thus deemed beneficial, which was also visible in the occurring shrinkage force. This change of the additives impact on the formulation was most likely the result of the interplay of an increased probability of chain propagation at low concentrations, even surpassing the values of the reference formulation, and significantly higher viscosity (and therefore lower probability of chain propagation) at higher concentrations. This was also visible in terms of time to reach 95% conversion ( $t_{95}$ ), depicted in Figure 3. As we had no means to discern a possible acceleration of the polymerization reaction by addition of this additive and a retardation caused by the increased viscosity, observed effects have to be considered as net effects. Mixtures containing PCL as additive expectedly showed a slight delay in  $t_{95}$  caused by an increase in viscosity, although this effect seemed less pronounced at higher concentrations. The effect was also visible with low concentrations of DVC but was counteracted at higher concentrations due to the copolymerization capability. Transfer agents, such as UDT, are known to cause retardation, accounting for the effects observed with higher concentrations of this additive.<sup>36</sup>

The reference mixture reached an overall DBC of 80%. The values for formulations containing 5–15 wt % PCL ranged around 83%, despite the increase in viscosity. This was a rather unexpected increase, regarding the fact that the additive did not participate in the polymerization reaction. However, as previously mentioned, a certain degree of prearrangement accompanied by the addition of substances with a tendency toward crystallization to a system prone to undergo phase separation can lead to this kind of behavior.<sup>39</sup> The highest conversion of 85% was reached with DVC\_15, which also happened to exhibit the lowest value of  $t_{95}$  of all mixtures. Formulations containing UDT showed DBC values from 81 to 83%, comparable to formulations containing PCL. In order to include considerations of kinetic data, the first derivative of the DBC curves was used to calculate the time to reach the maximum DBC rate ( $t_{max}$ ) and the according DBC (the detailed data set can be found in the Supporting Information, Table S1). We found that these data are very similar for physical and comonomeric additives (for different concentrations),  $t_{max}$  of about 17 s ( $\pm 3$  s) at conversions of 32% ( $\pm 6\%$ ), however, decreased to 13 s ( $\pm 3$  s) and 24% ( $\pm 6\%$ ), respectively, in case of the macromolecular chain extender UDT. This is a trend expected from complementary data acquired in these measurements. It has to be kept in mind that the (molar) thiol-ene ratio was held constant for all formulations, but the thiol in the reference mixture (TMPMP) was successively exchanged with UDT. Exchanging the low-molecular-weight trithiol with the long chain dithiol led to higher conversion rates in the initial phase of the polymerization; however, the maximum conversion rate (at  $t_{max}$ ) is attained earlier (compared to the reference mixture) and at lower conversions caused by a decrease of the probability of chain propagation owing a decreased chain mobility in the gelled state.

Since the gap size was held constant throughout the measurement, the resulting normal force ( $F_N$ ) necessary to counteract polymer shrinkage during photopolymerization was measured and used as an indicator for shrinkage stress.<sup>32</sup> The reference mixture developed a normal force around  $-21$  N and mixtures containing PCL or DVC showed similar values.

As depicted in Figure 3, UDT had a significant impact on the shrinkage force during polymerization. Within mixture UDT\_43 the shrinkage force ( $-F_N$ ) changed from 21 to 15 N (a decrease of 15%), while reaching high overall DBC. This was most likely the result of a combination of the CTA together with its high molecular weight causing significantly lower network density at the gel point.<sup>41</sup>

### Thermomechanical Properties

Photorheology provides valuable information on the crosslinking with all underlying processes; however, the change of the network architecture affects the final thermomechanical properties of the material, which have to be characterized by complementary methods.

DMTA measurements were performed to characterize the impact of the investigated additives on storage modulus ( $G'$ ) and the glass transition temperature ( $T_g$ ) of the modified polymer networks. This was of particular interest, as many toughness modifiers are known to have rather undesired influence on said properties.<sup>42</sup> A gradual drop of modulus was visible in all formulations, which was expected considering the increasing amount of high-molecular-weight modifiers. Results are summarized in Figure 3. Numerical data obtained through these measurements can be found in the Supporting Information (Table S2).

The unreactive modifier PCL showed the least alterations to the resulting polymer. This was expected as the linear polyester only influences the formed network physically by weak interactions and sterical hindrance. Low concentrations of PCL had close to no effect, while at increasing amounts the thermomechanical properties of PCL started to dominate the overall properties, leading to a decrease in  $T_g$ . Nevertheless, the value of  $T_g$  remained well above body temperature, which is crucial for the planned application.

Surprisingly, the addition of DVC led to an increase in  $T_g$  accompanied by a slight decrease in  $G'$ . Especially, DVC\_5 reached  $T_g$  increased by 10 °C and  $G'$  only lowered by around 10% compared to the reference mixture. This pronounced effect was already visible in the photorheology data, foremost regarding  $t_g$  and  $t_{95}$  values. Increasing amounts of additive again lead to a decrease in  $T_g$  but even DVC\_15 reached values above the reference formulation. This seemed to be a favorable combination of lowered network density while raising  $T_g$ . Similar findings were reported in literature with polymer blends containing PCL, where the introduction of a low amount of thermoplasts to a crosslinking polymer network resulted in improved homogeneity and thus superior (thermo-) mechanical properties.<sup>43,44</sup> This emphasizes that it is crucial to

ensure a chemical incorporation of the toughness modifier into the network to fully exploit beneficial impacts on the formed polymer architecture.

Formulations containing the urethane-based additive followed the expected trend of decreasing modulus and  $T_g$  with increasing amount of UDT. Already low amounts had significant impact on both values, becoming even more pronounced at higher concentrations. Formulation UDT\_43 only reached approximately 25% of the reference formulations' storage modulus. This goes in good accordance with the values obtained by photorheology, especially considering the delay in gelation, which influences the final material properties. Especially between UDT\_13 and UDT\_31, the drop in storage modulus at 37 °C was severe, as seen in Figure 3.

### Mechanical Properties

Polymer networks formed by chain-growth polymerization are known to be rather brittle due to their high crosslink density. Any means of regulating and loosening these networks usually result in tougher but softer materials. Although unmodified PCL cannot copolymerize with the vinyl ester monomer, blending was expected to enhance toughness, as the physically entangled structures are able to uncoil, providing additional means to dissipate stress.<sup>19,42</sup> The observed opacity of the PCL and DVC containing samples is indicative for phase separation, which is known to improve impact resistance as the crack propagating forces are efficiently dissipated between the two phases.<sup>19</sup> Since all additives were intended to improve impact toughness of the resulting polymers, Dynstat impact tests and tensile tests were performed. Numerical data obtained through these measurements can be found in the Supporting Information (Tables S3 and S4; Fig. S2).

The unmodified PCL additive showed rising values for impact strength with increasing amounts of additive. Alongside, both tensile strength ( $\sigma$ ) and elongation at break ( $\epsilon$ ) were similarly increased, which can be seen in Figure 3. The impact resistance results for PCL\_5 and PCL\_10 were basically identical, while differences in their tensile properties were more pronounced. Especially elongation at break of the materials benefits from the additive, as the introduced chains uncoil upon linear deformation, thus taking up the strain. This can be explained by the positive influence of a nonreactive additive in terms of chain confinement, similar to nanocomposites, where domains arrange within the polymer as result of restricted chain mobility.<sup>45</sup> These effects were already responsible for the impact on the probability of chain propagation found in photorheology measurements. This arrangement can promote phase separation, leading to improved mechanical properties. The highest amount of additive resulted in the best values for both impact resistance and tensile test results. A further increase of additive was avoided, as the thermomechanical properties would further decrease, making the resulting materials no longer suitable for the intended application. Furthermore, processing in conventional L-AMT system at room temperature would be impossible, especially considering filled systems, as they are limited to a maximum viscosity of 20 Pa s.<sup>46</sup>

Similar effects were observed with DVC as additive, where again impact resistance and tensile properties increase with the amount of additive. The impact resistance values for DVC\_5 and DVA\_10 did not vary considerably, as seen in Figure 3, but were slightly better than their PCL analogs. DVC\_15 yielded the highest impact resistance value but it must be taken into account that impact tests with unnotched samples are generally accompanied with high SD. Concerning tensile strength, as can be seen in Figure 3, the optimum was at 10 wt %wt % DVC, as the value started to drop again at higher concentrations, although photorheology results showed further increase in the probability of chain propagation. Comparable effects were observed in a previous study with various thiols, where a decrease of tensile strength was measured above a certain thiol concentration.<sup>30</sup> Exceeding the optimal amount of thiol results in high chain flexibility and rather low network density, causing a decrease in modulus and tensile strength. Considering a future application in filled systems, a drop in modulus of around 20% was deemed acceptable, as the incorporation of nanoparticles is expected to increase these values.<sup>19</sup>

As anticipated, the urethane group containing additive UDT with its cyclic motifs significantly improved impact resistance, as seen in Figure 3. The intermolecular forces, introduced by the urethane moieties, allowed the system to absorb energy without actually breaking covalent bonds.<sup>11</sup> Contrary to the other additives, the lowest investigated amount of 1 mol % showed no visible improvement in terms of impact toughness, thus rather high amounts had to be added to the reference formulation. At 3 mol %, clear enhancements of impact toughness were visible, which can also be seen in the tensile test data, summarized in Figure 3, where a steady increase of elongation at break with additive concentration is depicted. By comparison, the UDT did increase elongation at break up to 11% sacrificing around 50% the initial tensile strength. The resulting network was too loose due to the high amount of UDT, causing those rather poor values for tensile strength. These findings are in good accordance with literature.<sup>20,47</sup> The obtained results showed that UDT did increase toughness, but is nevertheless unfit to be used as additive in this specific application due to pronounced softening and weakening of the resulting material.

### CONCLUSIONS

We have investigated three toughness-improving additives for vinyl ester-based thiol-ene photoresins containing a PCL motif. All additives improved impact toughness, which was the primary intention of the experimental setup.

The addition of the commercially available, unmodified PCL provided a valuable increase in material toughness, achieved by physical entanglement with the polymer network. Tensile tests also showed an increase in elongation at break without forfeiting tensile strength. The only setback was found within the analysis of thermomechanical properties, revealing a slight decrease in glass transition temperature.

With the introduction of copolymerizable end groups through the synthesis of the according DVC, slightly better results were obtained in terms of impact resistance. Elongation at break increased considerably with increasing amount of DVC, again while maintaining the initial tensile strength. The highest concentration of DVC nearly doubled the initial value of elongation at break. Most beneficial was the addition of DVC on the thermomechanical properties, resulting in an increase in glass transition temperature. A trade-off has to be made from an economical point of view, considering the benefits gained from the chemical modification of the native PCL.

The UDT, although having distinct impact on the reactivity, did not excel within these studies. Despite UDT improved both impact resistance and elongation at break, especially at higher concentrations, the loss in tensile strength and especially glass transition temperature was too severe. Thus, only low amounts of this additive are considered suitable, preferably in filled systems, to keep the formulation processable in terms of viscosity and maintain reasonable mechanical properties for bone tissue engineering.

DVC in concentrations of 10–15 wt % showed the best additive performance overall, with high impact strength and elongation at break, higher glass transition temperature compared the unmodified resin, while exhibiting similar reactivity, conversion and tensile strength.

The next steps in order to confirm eligibility for the application of the above described additives for bone tissue engineering is the fabrication of scaffolds using DLP-SLA. Moreover, the degradation characteristics of photopolymer networks containing the examined additives have to be investigated.

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