Supporting Information

Photopolymers based on boronic esters for enhanced degradation of 3D-printed scaffolds

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1. Synthesis of Monomers and Thiols for Degradable Networks

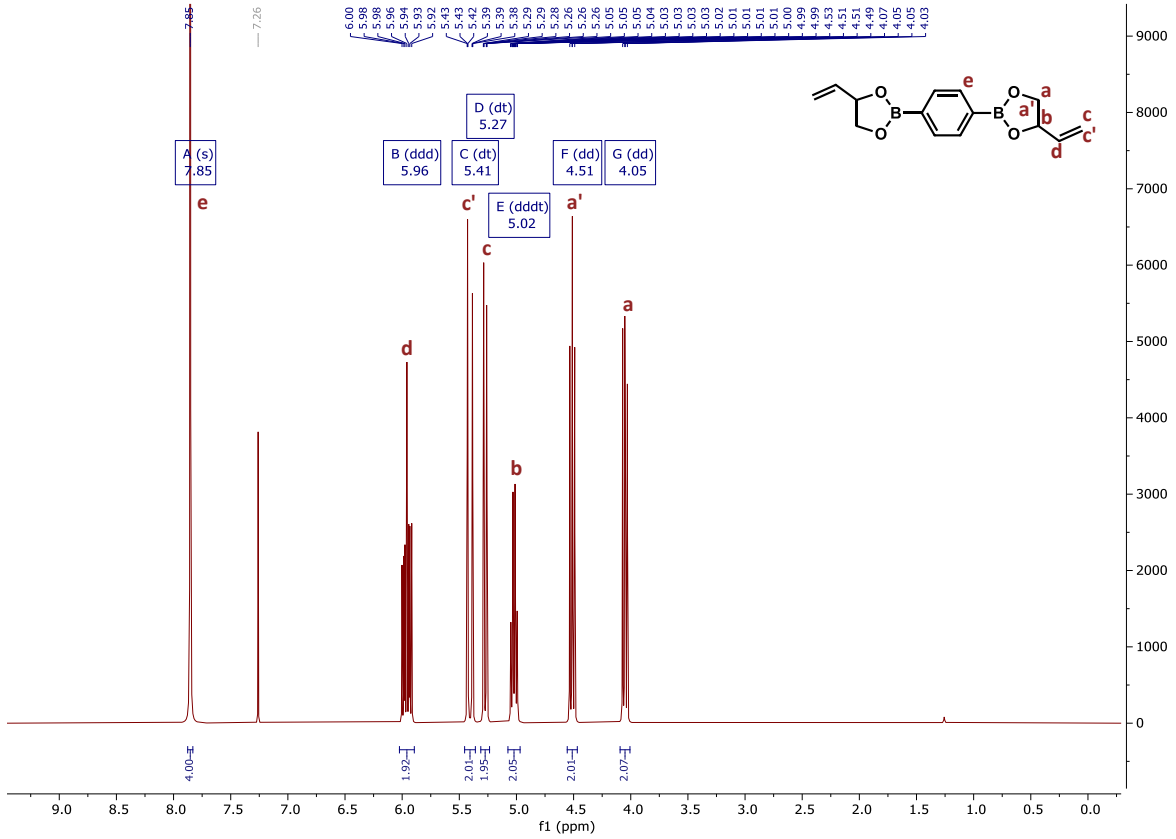

Figure S 1: ^{1}H-NMR of VDB.

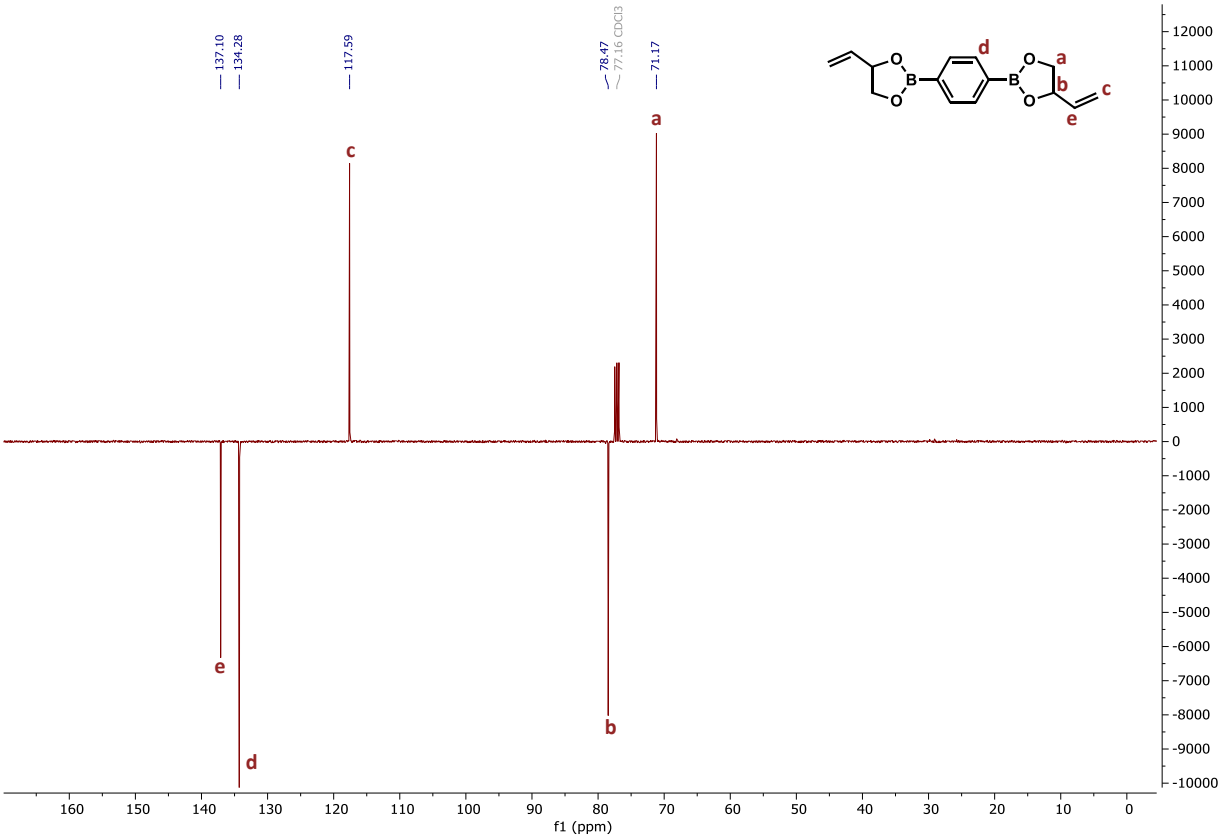

Figure S 2: ^{13}C-APT-NMR of VDB.

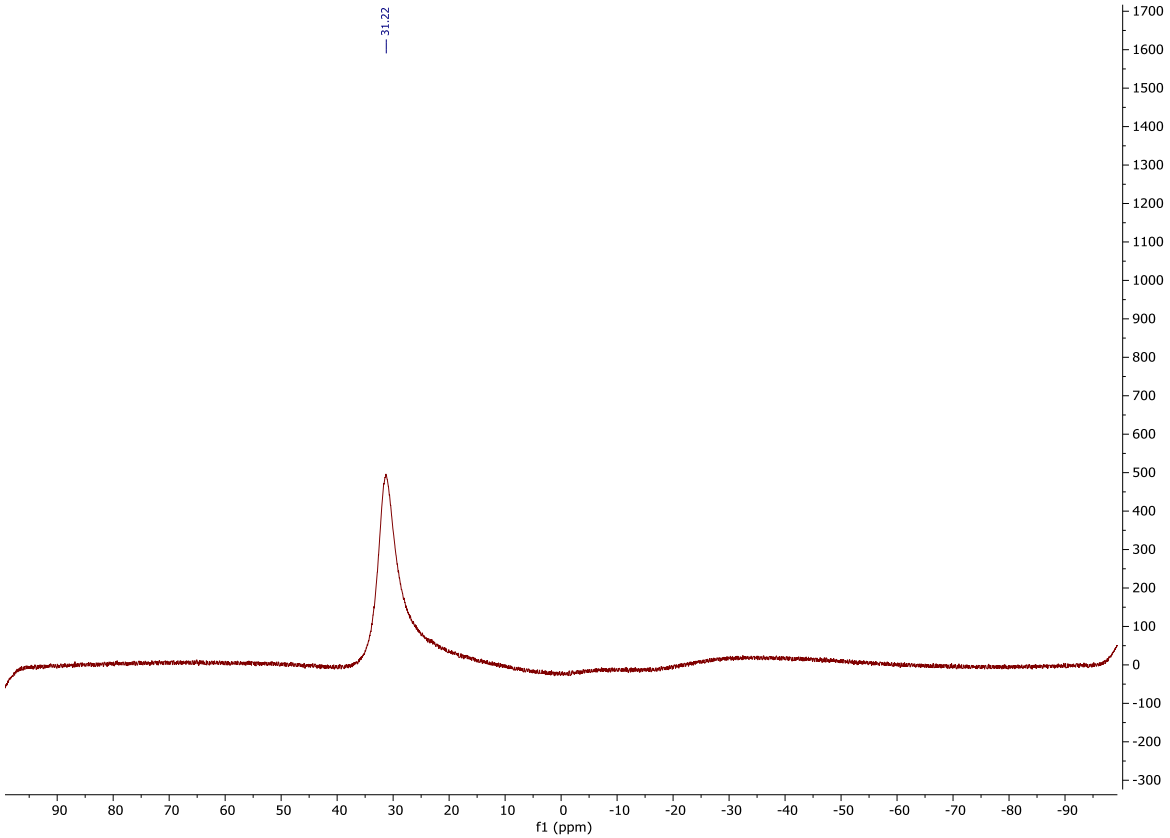

Figure S 3: ^{11}B-NMR of VDB.

2. Cytotoxicity Tests

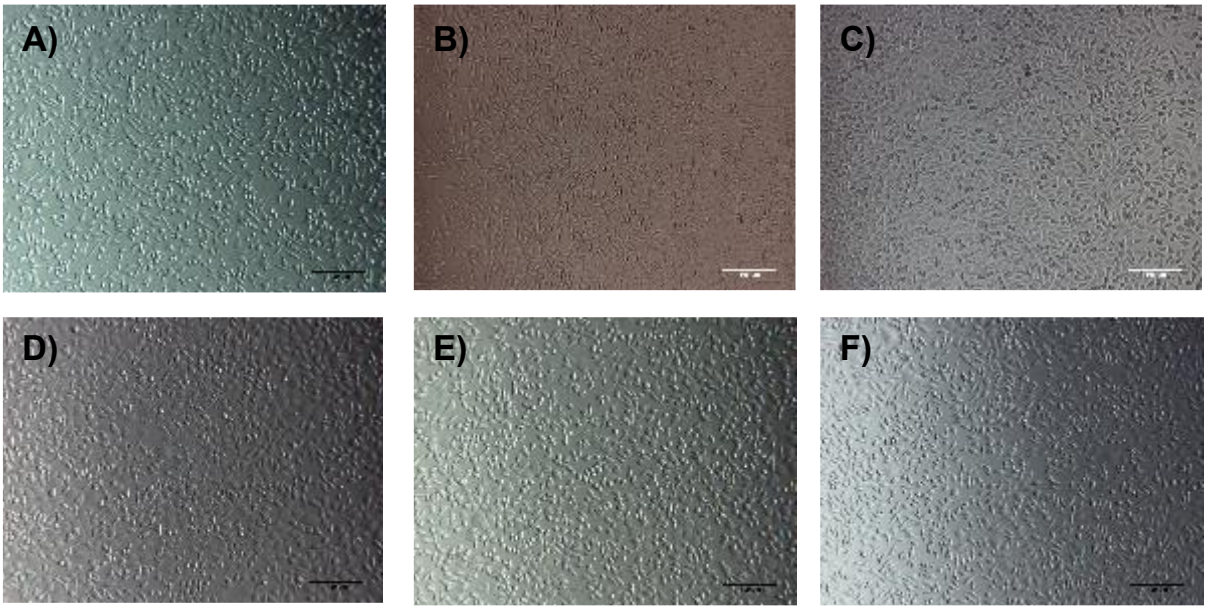

Figure S 4: Qualitative assessment of cell morphology according to ISO 10993-5 under the microscope after 24 h of incubation with the respective substances A) 10.0 mM VDB, B) 2.5 mM ADB, C) 10 mM VSA C D) 2.5 mM TMT compared to the control cells treated with E) PBS buffer or F) 1% DMSO.

Table S 1. Cell viabilities at the different concentrations of the test substances measured by fluorescence. Values represent the mean of three measurements.

substance	cell viability 10 mM [%]	cell viability 7.5 mM [%]	cell viability 5 mM [%]	cell viability 2.5 mM [%]
VDB	59.3	72.1	75.9	70.1
ADB	39.5	25.2	32.6	51.2
VSA	91.3	105.5	119.7	121.6
TMT	21.4	23.9	32.3	72.7

3. Network formation

Table S 2: Viscosity of different formulations containing each monomer and the thiol TMT in a double bond to thiol ratio of 1:1 with 1 w% Ivocerin and 0.02w% pyrogallol at 25 °C and the printing temperature of 55 °C.

sample	$\eta_{25\,°C}$ [mPa s]	$\eta_{55\,°C}$ [mPa s]
VDB	*	506
ADB	646	164
VSA	525	107

*No viscosity could be determined, as crystallization of the formulation occurred.

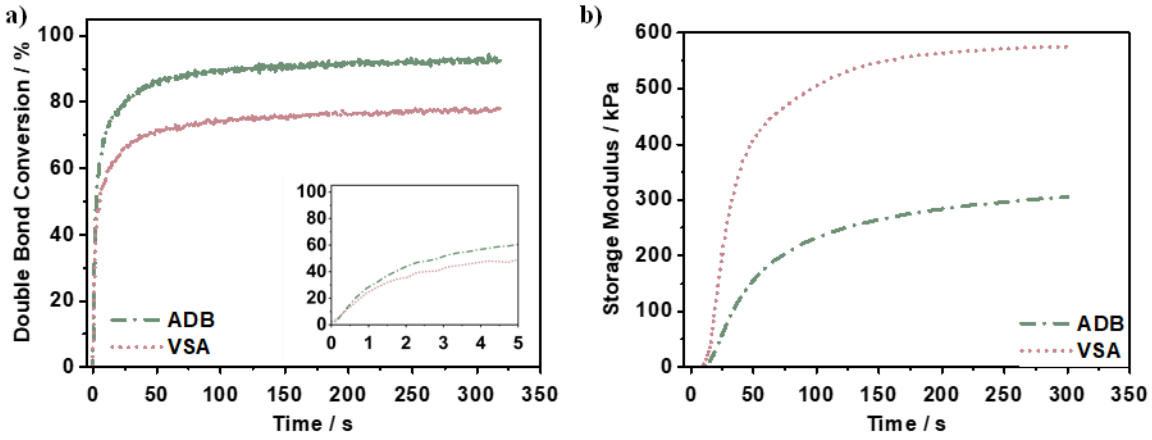

Figure S 5: Results of photorheological analysis of formulations containing each monomer and the crosslinking thiol TMT in an equimolar ratio of double bonds to thiol groups; Comparison of exemplary curves of a) double bond conversion and b) storage modulus over time of ADB (green, dash-dotted) and VSA (pink, dotted) at 25 °C. For VDB no measurements could be conducted at 25 °C, as crystallization of the formulation occurred.

Table S 3: Detailed results of the RT-NIR photorheology measurements of different formulations containing each monomer and the thiol TMT in a double bond to thiol ratio of 1:1 with 1 w% Ivocerin and 0.02w% pyrogallol at 25 °C. Results for time of gelation t_{gel}, time to attain 95% of the final conversion t_{95}, double bond conversion at the gel point DBC_{gel}, final storage modulus G'_{max} and maximum normal force $F_{N,max}$ and rate of polymerization R_p.

sample	R_p [% s^{-1}]	STD	t_{gel} [s]	STD	DBC_{gel} [%]	STD	t_{95} [s]	STD	DBC_{final} [%]	STD	G'_{max} [kPa]	STD	$F_{N,max}$ [N]	STD
VDB	*	*	*	*	*	*	*	*	*	*	*	*	*	*
ADB	24.7	1.5	33.7	1.2	82.6	0.1	65.0	2.0	92.4	0.2	332.0	82.6	-9.3	-1.7
VSA	21.7	1.0	25.3	0.6	66.8	0.2	74.8	3.9	77.9	0.3	547.2	40.0	-14.9	-2.5

*No value could be determined, as crystallization of the formulation occurred.

Table S 4:Detailed results of the RT-NIR photorheology measurements of different formulations containing each monomer and the thiol TMT in a double bond to thiol ratio of 1:1 with 1 w% Ivocerin and 0.02w% pyrogallol at 55 °C. Results for time of gelation t_{gel}, time to attain 95% of the final conversion t_{95}, double bond conversion at the gel point DBC_{gel}, final storage modulus G'_{max} and maximum normal force $F_{N,max}$ and rate of polymerization R_p.

sample	R_p [% s^{-1}]	STD	t_{gel} [s]	STD	DBC_{gel} [%]	STD	t_{95} [s]	STD	DBC_{final} [%]	STD	G'_{max} [kPa]	STD	$F_{N,max}$ [N]	STD
VDB	37.6	1.2	11.0	0	87.1	0.7	21.9	1.8	96.4	0.3	239.8	6.2	-7.2	-0.5
ADB	40.7	2.6	7.0	0	85.1	0.1	30.6	1.3	95.0	0.1	190.8	5.6	-6.5	-0.1
VSA	37.4	0.6	11.0	0	74.4	0.2	52.9	1.1	89.2	0.8	169.9	11.3	-8.5	-0.4

4. Network Characterization

Table S 5: Results of DMTA measurements for VDB-, ADB- compared to VSA-based networks; Results for glass transition temperature T_g, storage modulus at room temperature $G'_{25°C}$ and body temperature $G'_{37°C}$ and storage modulus at the rubber plateau G'_R.

network	T_g [°C]	$G'_{25°C}$ [MPa]	$G'_{37°C}$ [MPa]	G'_R [MPa]
VDB	70	1340	1280	-
ADB	33	459	5	-
VSA	74	1640	1590	8

Table S 6: Detailed results of the tensile test measurements for VDB-, ADB- and the reference VSA-based network. Results for tensile strength σ_M, elongation at break ε_B, tensile toughness U_T and slope of the curves.

sample	σ_M [MPa]	STD	ε_B [%]	STD	U_T [MJ/m^3]	STD	slope [MPa]	STD
VDB	67.0	0.4	11.0	1.1	4.7	0.6	1310	50
ADB	14.6	2.3	313.1	30.3	20.8	4.0	310	25
VSA	68.5	1.8	10.5	1.4	4.6	0.7	1580	50

5. Degradation of Boronic Ester-containing Networks

Swelling and mass loss of the materials was calculated using the following formulas:

$$\textbf{Swelling}\ [\%] = \frac{\mathbf{m_t - m_{dry}}}{\mathbf{m_{dry}}} \cdot \mathbf{100}$$

$$\textbf{Mass change}\ [\%] = \frac{\mathbf{m_{dry} - m_0}}{\mathbf{m_0}} \cdot \mathbf{100}$$

Equation S 1: Calculation of swelling and mass change m_{change}; m_t…mass of the blot dried sample at the time t; m_{dry}…mass of the sample after drying to constant weight; m_0…initial mass of sample

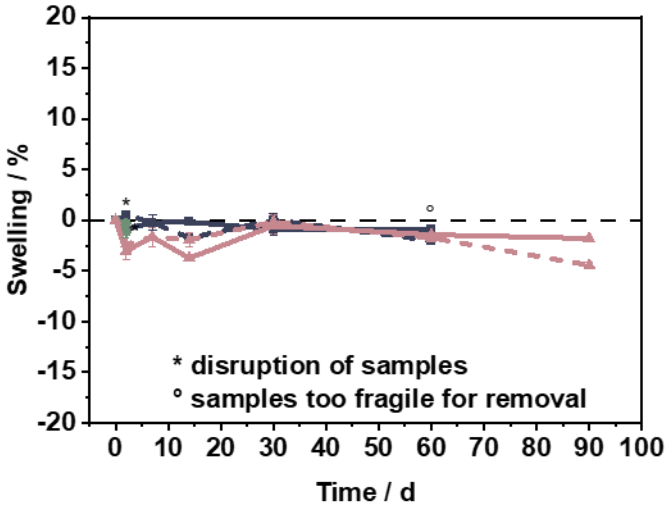

Figure S 6: Swelling versus time of polymer networks under physiological conditions (PBS, pH = 7.4, solid line) and acidic conditions (acetate buffer, pH = 4, dashed line) for VDB- (blue), ADB- (green) and the reference VSA- based network (pink); *no samples could be removed as disruption of the specimens occurred.

A slight decrease in swelling was observed for all materials and conditions over the course of the experiment. These results can be explained by residual salt traces of the buffer solutions in the test vials, which were weighed in combination with the dried sample to determine the dry weight. This was done for means of consistency as some samples disrupted during the experiment or became too fragile for removal due to the small sample sizes used (~50 mg). Nevertheless, maximum negative values of 2% were observed for B-containing materials, which is marginal considering the low sample masses of approx. ~50 mg. For the materials containing VSA, the negative values from 0.5 to 4.4% can be additionally explained by the irreversible water uptake of the networks of 2-3% over the course of the experiment. Hence, these results comprehensively demonstrate, that negligible swelling occurred for all materials and that water uptake was limited.

Table S 7: Detailed results of the degradation studies for the VDB-based network under physiological conditions (PBS, pH = 7.4) and acidic conditions (acetate buffer, pH = 4). *Samples too fragile for removal.

sample	pH	Time [d]	Swelling [%]	STD	Mass change [%]	STD
VDB	7.4	**2**	-0.9	0.3	-23.7	6.3
		7	-0.2	0.7	-54.7	0.0
		14	-0.2	0.3	-65.2	0.0
		30	-0.9	0.7	-67.3	1.9
		60	-0.9	0.4	-78.7	0.1
		90	*	*	-75.7	0.0
	4	**2**	0.5	0.1	-24.7	2.5
		7	-0.2	0.1	-63.6	9.2
		14	-1.8	0.4	-70.7	0.0
		30	0.0	0.7	-89.4	2.3
		60	-2.0	0.0	-87.4	5.7
		90	*	*	-84.2	0.5

Table S 8: Detailed results of the degradation studies for the ADB-based network under physiological conditions (PBS, pH = 7.4) and acidic conditions (acetate buffer, pH = 4). °Disruption of specimens occurred.

sample	pH	Time [d]	Swelling [%]	STD	Mass Change [%]	STD
ADB	7.4	2	0.0	0.0	0.0	0.0
		7	-1.2	0.6	-57.1	1.5
		14	°	°	-90.0	2.0
		30	°	°	-91.1	2.1
		60	°	°	-92.0	1.2
		90	°	°	-89.2	1.2
	4	2	0.0	0.0	0.0	0.0
		7	-0.3	0.0	-51.4	1.7
		14	°	°	-85.0	2.0
		30	°	°	-88.6	0.2
		60	°	°	-96.7	1.3
		90	°	°	-92.8	2.2

Table S 9: Detailed results of the degradation studies for the VSA-based network under physiological conditions (PBS, pH = 7.4) and acidic conditions (acetate buffer, pH = 4).

sample	pH	Time [d]	Swelling [%]	STD	Mass Change [%]	STD
VSA	7.4	**2**	-3.0	0.8	0.0	0.0
		7	-1.7	1.0	3.1	0.5
		14	-3.7	0.3	2.9	0.7
		30	-0.6	0.8	3.2	0.6
		60	-1.4	0.0	2.4	1.0
		90	-1.8	0.0	2.8	0.1
	4	**2**	-2.4	0.9	0.0	0.0
		7	-1.7	1.0	3.2	1.1
		14	-1.9	0.8	2.4	1.0
		30	-0.2	0.7	2.2	1.0
		60	-1.8	0.3	1.2	0.9
		90	-4.4	0.3	2.8	0.4

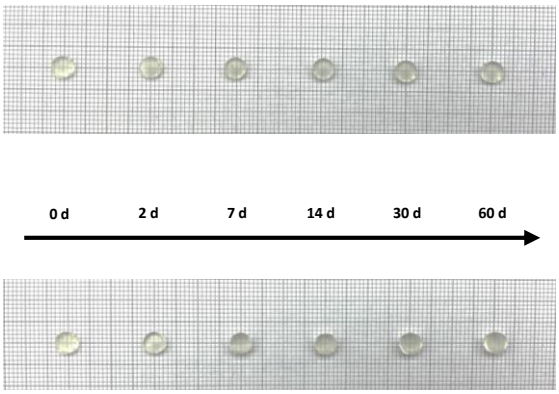

Figure S 7: Photographs of the VSA-based network at different degradation times under physiological conditions (PBS, pH = 7.4, upper photograph) and acidic conditions (acetate buffer, pH = 4, lower photograph) depicting that no degradation of the reference network occurs.

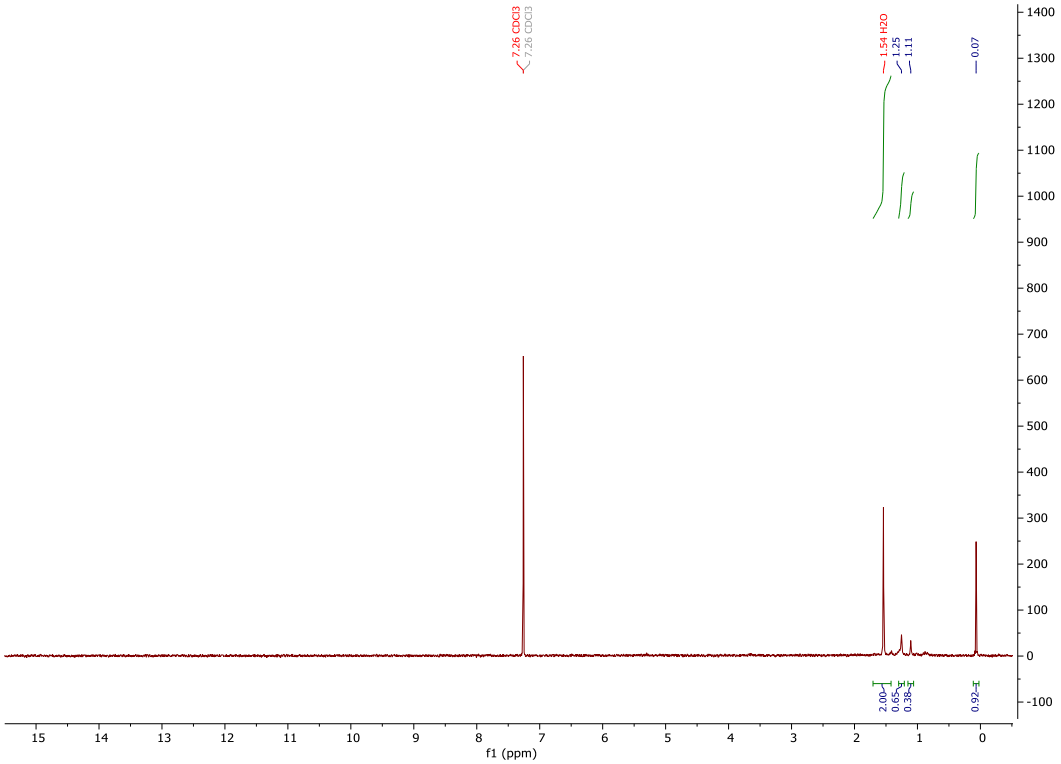

Figure S 8: ^{1}H-NMR (400 MHz) of buffer solution extracted with $CDCl_3$ after 3 M of degradation studies for the VSA-based material at a pH of 7.4.

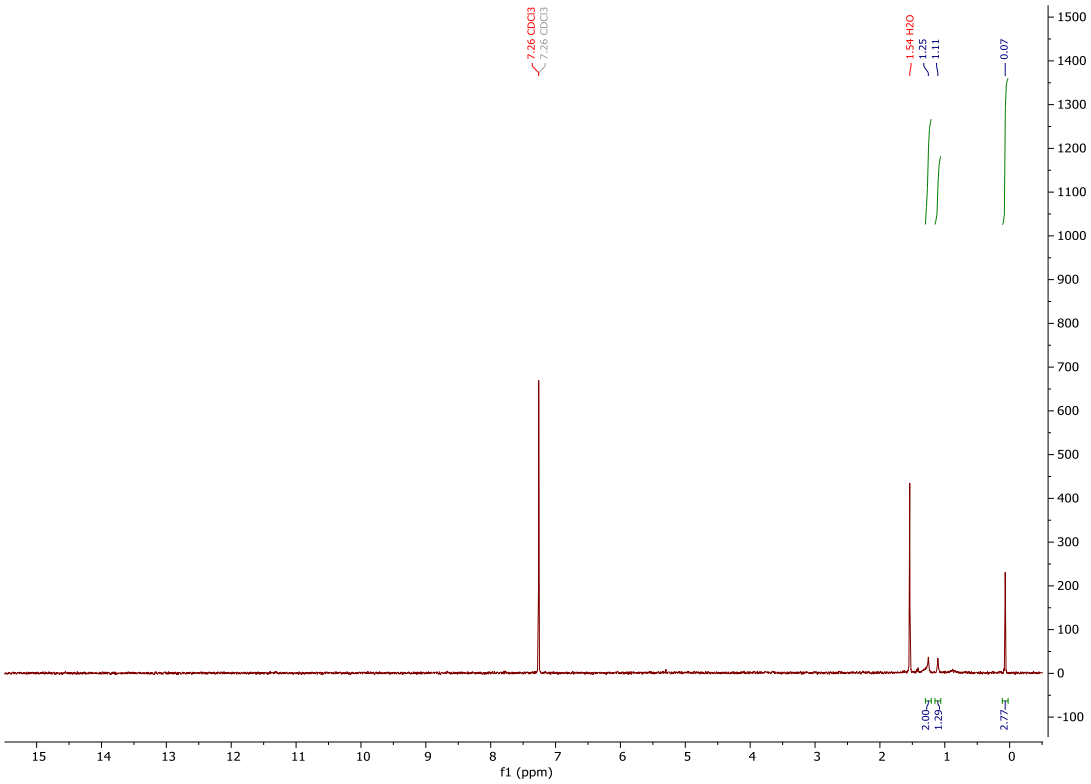

Figure S 9: ^{1}H-NMR (400 MHz) of buffer solution extracted with $CDCl_3$ after 3 M of degradation studies for the VSA-based material at a pH of 4.

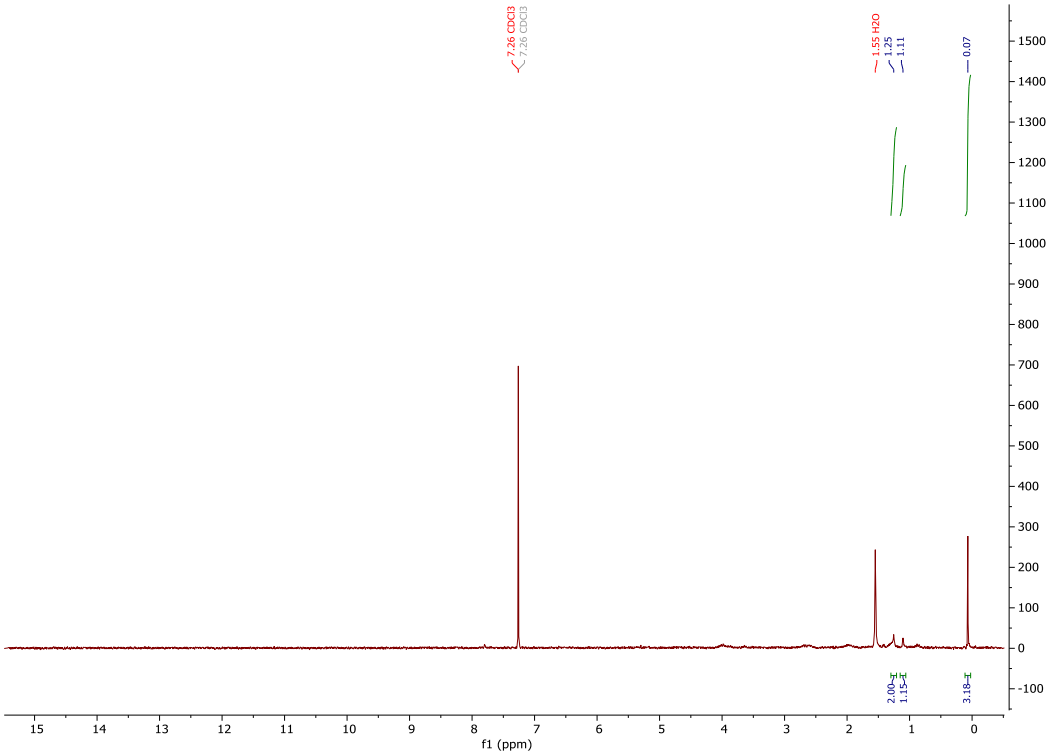

Figure S 10: ^{1}H-NMR (400 MHz) of buffer solution extracted with $CDCl_3$ after 3 M of degradation studies for the VDB-based material at a pH of 7.4.

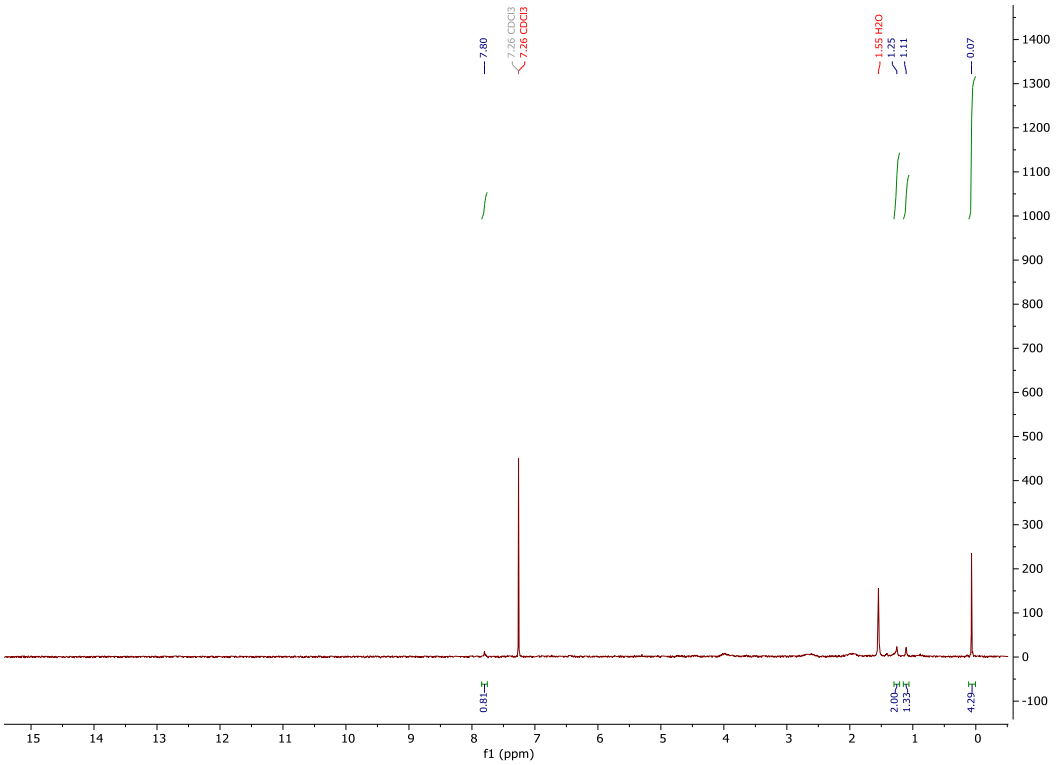

Figure S 11: ^{1}H-NMR (400 MHz) of buffer solution extracted with $CDCl_3$ after 3 M of degradation studies for the VDB-based material at a pH of 4.

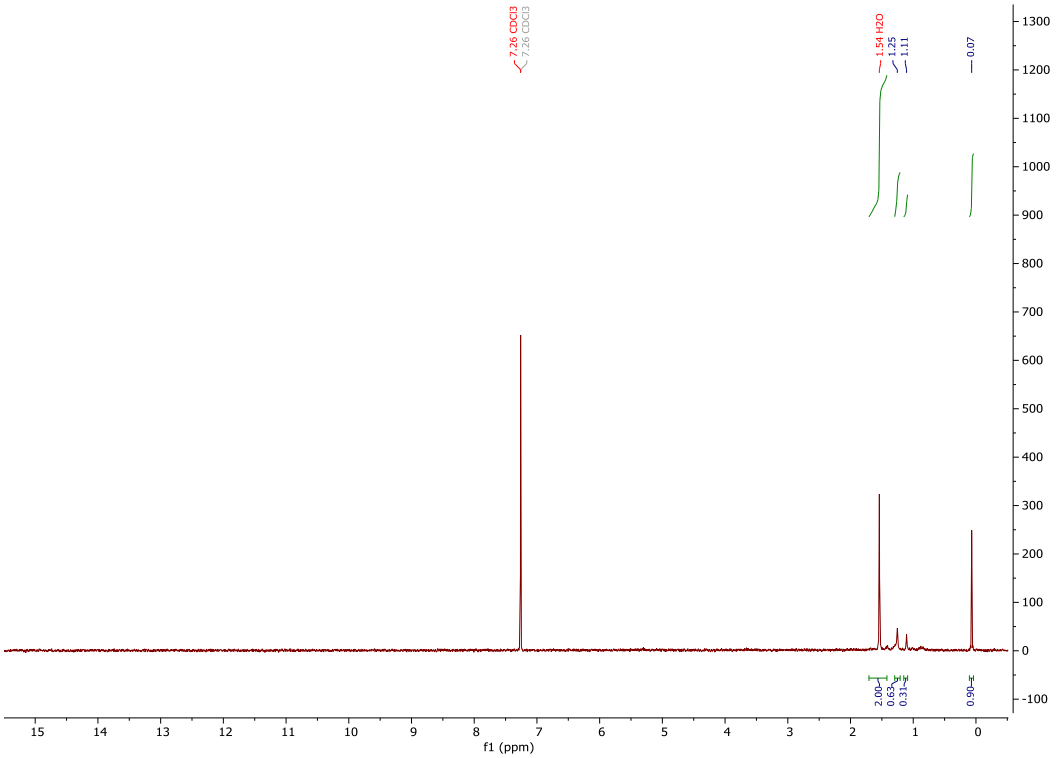

Figure S 12: ^{1}H-NMR (400 MHz) of buffer solution extracted with $CDCl_3$ after 3 M of degradation studies for the ADB-based material at a pH of 7.4.

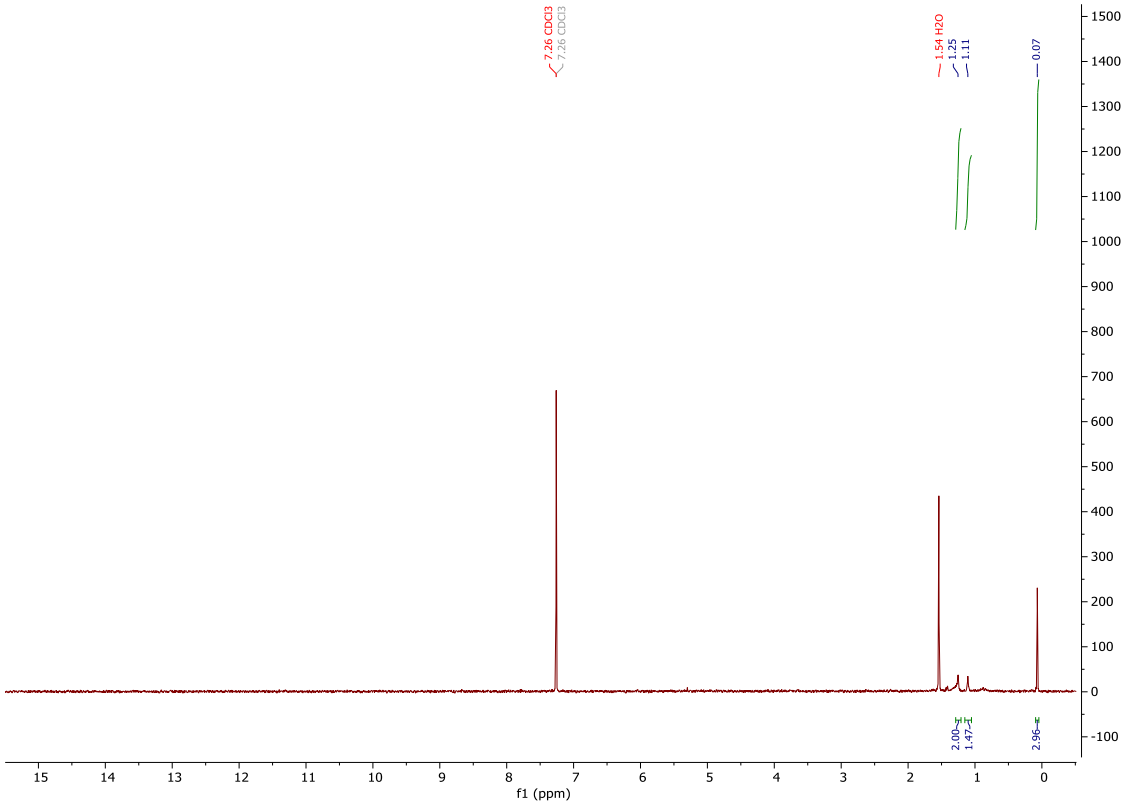

Figure S 13: ^{1}H-NMR (400 MHz) of buffer solution extracted with $CDCl_3$ after 3 M of degradation studies for the ADB-based material at a pH of 4.

6. Degradation under basic conditions

To determine possible differences to the degradation under physiological and acidic conditions present in the body, also the degradation of the materials under basic conditions was studied. For this, a basic buffer medium was used, namely a carbonate-bicarbonate buffer, which was prepared from 3.88 g sodium bicarbonate and 6.71 g sodium carbonate dissolved in 1 L of deionized water.

Table S 10: Detailed results of the degradation studies for the VDB-based network under basic conditions (carbonate-bicarbonate buffer, pH=10).°Disruption of specimens occurred.

sample	pH	Time [d]	Swelling [%]	STD	Mass change [%]	STD
VDB	10	2	°	°	-92.90	0.51
		7	°	°	-89.58	5.42
		14	°	°	-87.42	6.66
		30	°	°	-90.45	0.97
		60	°	°	-90.47	1.84
		90	°	°	-90.48	0.70
ADB	10	2	°	°	-60.00	2.00
		7	°	°	-87.00	2.00
		14	°	°	-88.91	5.70
		30	°	°	-97.59	0.22
		60	°	°	-99.78	1.53
		90	°	°	-92.40	2.95
VSA	10	2	-1.39	0.24	2.90	0.40
		7	-1.95	0.31	3.28	0.52
		14	-1.65	1.27	1.91	1.52
		30	0.46	0.20	0.68	0.47
		60	0.17	0.15	1.42	0.14
		90	-3.22	0.88	4.74	0.91

Degradation studies under basic conditions revealed no mass loss but a slight irreversible water-uptake for the reference material containing VSA. For the materials containing the boronic esters VDB and ADB full disruption of samples occurred within 1 d, owing to the Lewis acidity of the boronic ester moiety, able to react with OH^- under the formation of ionic borate species, which are water soluble. This results in fast mass changes within the first week of almost 90% for both materials, which is significantly accelerated compared to the degradation rates at physiological and acidic conditions.

7. Sterilization of VDB-based materials

Table S 11: Results of DMTA measurements for VDB-based networks before (Ref) and after sterilization (EO, low γ, high γ); Results for glass transition temperature T_g, storage modulus at room temperature $G'_{25°C}$ and body temperature $G'_{37°C}$ and storage modulus at the rubber plateau G'_R.

sample	T_g [°C]	$G'_{25°C}$ [MPa]	$G'_{37°C}$ [MPa]	fwhm [°C]	G'_R [MPa]
Ref	70	1339	1276	10	-*
EO	67	1337	1286	10	-*
low γ	75	1229	1187	11	-*
high γ	70	1287	1241	11	-*

Table S 12: Results of tensile tests for VDB-based networks before (Ref) and after sterilization (EO, low γ, high γ); Results for tensile strength σ_M, elongation at break ε_B, tensile toughness U_T and slope of the curves.

sample	σ_M [MPa]	STD	ε_B [%]	STD	U_T [MJ/m^3]	STD	slope [MPa]	STD
Ref	67.0	0.4	11.0	1.1	4.7	0.6	1310	50
EO	71.7	1.8	11.2	1.2	5.17	0.66	1274	26
low γ	71.1	1	12.6	1.7	5.91	0.90	1280	12
high γ	68.1	0.8	9.4	1.2	4.17	0.78	1254	31

8. Creep tests

Creep tests were done on a TA Instruments DMA 850 in bending mode at a load stress of 1 MPa. Support span was 10 mm, the specimens had a thickness of 0.8 mm and a width of 5 mm. Tests were carried out at 37 °C.

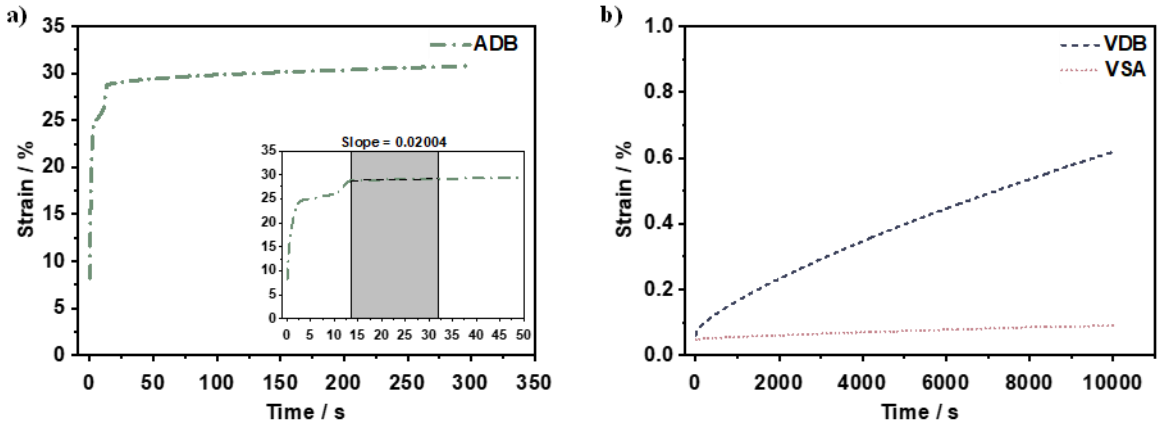

Figure S 14: Results of creep tests of strain over time for a) ADB (green, dash-dotted) and b) VDB (blue, striped) and (VSA (pink, dotted) at 37 °C and a load of 1 MPa. For ADB significant creep occurred, resulting in the sample falling off the device during the measurements. Hence, tests could only be performed for 300 s.

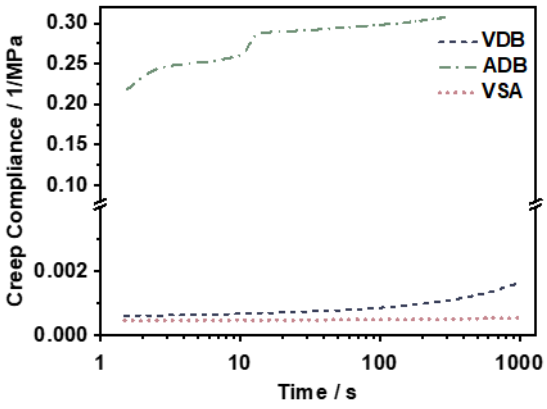

Figure S 15: Results of creep tests of creep compliance over time for a) ADB- (green, dash-dotted) and b) VDB- (blue, striped) and VSA-based materials (pink, dotted) at 37 °C and a load of 1 MPa. For ADB significant creep occurred, resulting in the sample falling off the device during the measurements. Hence, tests could only be performed for 300 s.

Table S 13: Steady state creep rate dε/dt for VDB-, ADB- and the reference VSA-based network.

sample	dε/dt [s^{-1}]
VDB	$5.15 \cdot 10^{-3}$
ADB	2.00
VSA	$4.10 \cdot 10^{-4}$