

Supporting Information- Photopolymerizable Precursors for Degradable Biomaterials Based on Acetal Moieties

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Synthesis of Reference Systems

Synthesis of the reference system 1,4-benzenedimethanol dimethacrylate (DMMA)

For the synthesis of DMMA, 1,4-benzenedimethanol (3.0 g, 21.7 mmol), MEHQ (1000 ppm), phenothiazine (300 ppm) and triethylamine (6.59 g, 65.1 mmol) were dissolved in a three-necked flask in dry THF (200 mL), cooled with an ice bath and purged with argon. Freshly distilled methacryloyl chloride (5.45 g, 52.1 mmol) was diluted in 20 mL dry THF and added dropwise to the reaction mixture. The reaction mixture was stirred for 1 h at 0 °C. Then, the reaction mixture was stirred for additional 2 days at room temperature. The reaction mixture was filtered to remove the salts. The reaction mixture was washed with sat. NH₄Cl (3 x 30 mL) and brine (2 x 20 mL). The combined organic phases were dried with Na₂SO₄, filtered and the solvent was removed under reduced pressure. The crude product was recrystallized in methylene chloride to yield the final product as yellow crystals in 3.2 g (53% calculated yield). m.p.: 65 – 67 °C. ¹H NMR (400 MHz, DMSO-*d*₆) δ (ppm): 7.39 (s, 4H, Ar-H), 6.07 – 6.08 (m, 2H, =CH₂), 5.70 – 5.69 (m, 2H, =CH₂), 5.17 (s, 4H, -Ar-CH₂-), 1.90 - 1.89 (m, 6H, -CH₃). ¹³C-NMR (400 MHz, DMSO-*d*₆) δ (ppm): 166.3, 136.0, 135.8, 127.9, 126.1, 65.5, 17.9.

Synthesis of 2,4,8,10-tetraoxaspiro[5.5]undecane-3,9-diyl)bis(2-methylpropane-2,1-diyl) dipropionate (EIBSPG)

β3,β3,β9,β9-tetramethyl-2,4,8,10-tetraoxaspiro[5.5]undecane-3,9-diethanol (Isobutyril-SPG, **IBSPG**) and 4-dimethylaminopyridine (DMAP) were dissolved in 260 mL dry THF in a three-necked round-bottomed flask and the apparatus was flushed with argon. Propionyl chloride was added dropwise and a white salt precipitated. The reaction mixture was stirred at room temperature for 18 hours. The salt was removed by filtration and the reaction mixture was washed with saturated NH₄Cl solution (2 x 30 mL) and brine (2 x 30 mL). Then the combined organic layers were dried over anhydrous Na₂SO₄. Afterwards the solvent was evaporated and a light-pink solid was obtained. The resulting powder was recrystallized in PE to isolate the product as light-pink powder in 5.61 g (82% calculated yield). m.p.: 86.2-87.2 °C. ¹H-NMR (400 MHz, CDCl₃) δ (ppm): 4.50 (dd, *J* = 11.4, 2.5 Hz, 2H, OCH₂C), 4.24 (s, 2H, OCHO), 3.92 (s, 4H, CH₂OC=O), 3.56 (dd, *J* = 11.5, 2.6 Hz, 2H, OCH₂C), 3.50 – 3.42 (m, 2H, OCH₂C), 3.30 (d, 2H, *J* = 11.4 Hz, OCH₂C), 2.34 (q,

4H, $J = 7.6$ Hz, $\text{CH}_2\text{-CH}_3$), 1.15 (t, 6H, $J = 7.6$ Hz, $\text{CH}_2\text{-CH}_3$), 0.95 (d, 12H, $J = 4.6$ Hz, $\text{C}(\text{CH}_3)_2$). ^{13}C -NMR (400 MHz, CDCl_3) δ (ppm): 174.5, 105.1, 70.7, 70.3, 69.3, 38.7, 32.7, 19.6, 19.4, 9.4.

Investigation of Network Formation with RT-NIR-Photorheology.

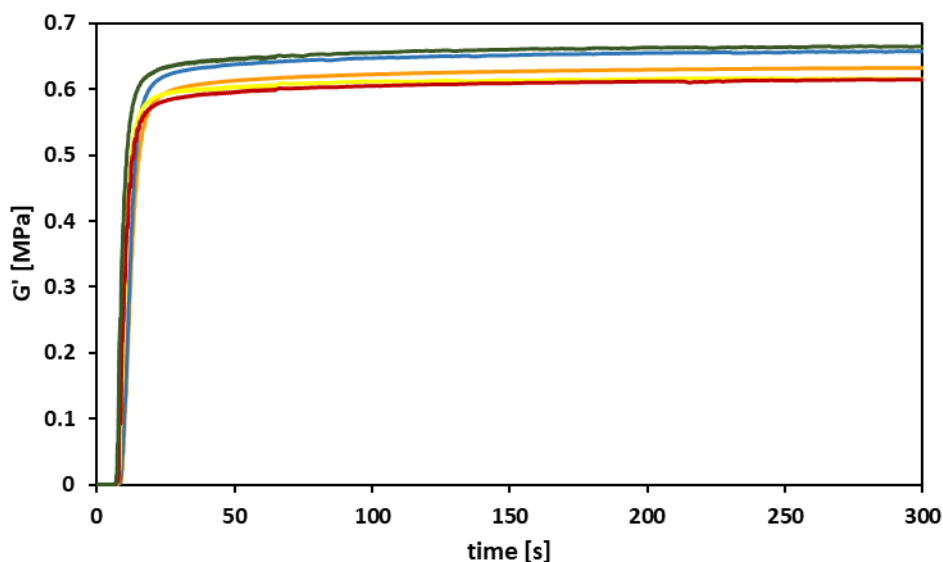


Figure S. 1: Results of RT-NIR-photorheology measurements: Storage modulus G' for formulation contained the reference system/ acetal-based monomer and NAM (1:4 DB-ratio), and 1 mol% PI. D3MA in orange (—), VMA in dark blue (—), DMMA in yellow (—), T5MA in dark green (—) and MB5MA in dark red (—). (Gray dashed line indicates body temperature).

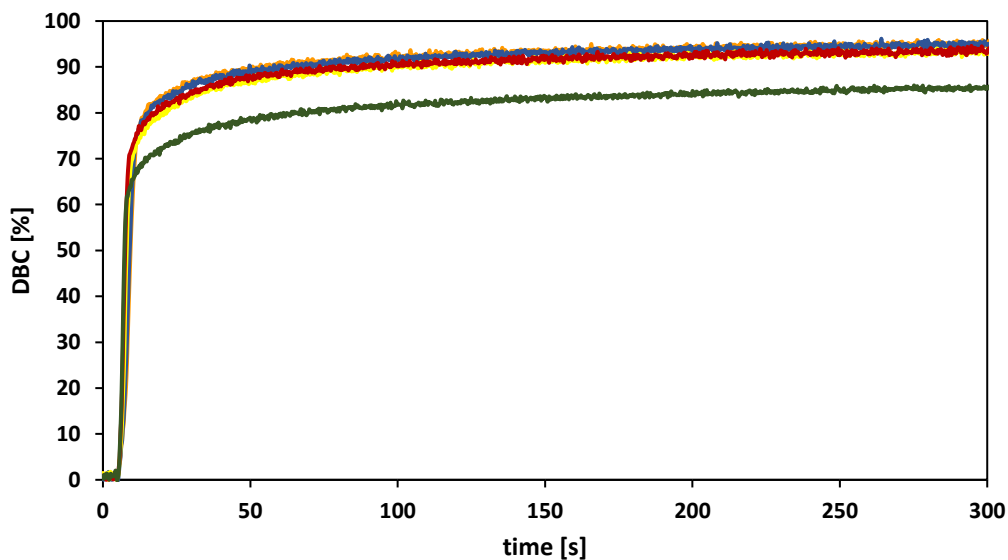


Figure S. 2: Results of RT-NIR-photorheology measurements: final Double Bond Conversion (DBC) for formulation contained the reference system/ acetal-based monomer and NAM (1:4 DB-ratio), and 1 mol% PI. D3MA in orange (—), VMA in dark blue (—), DMMA in yellow (—), T5MA in dark green (—) and MB5MA in dark red (—). (Gray dashed line indicates body temperature).

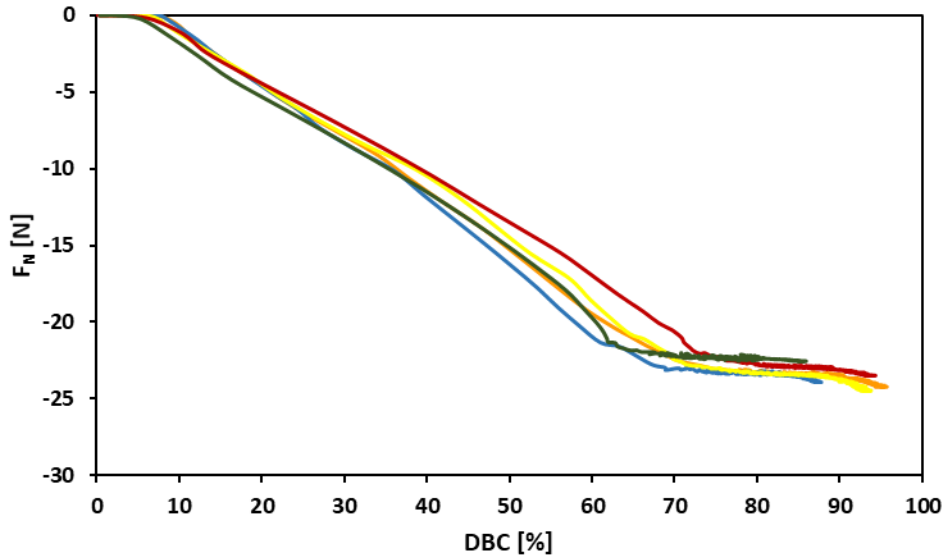


Figure S. 3: Results of RT-NIR-photorheology measurements: Normal Force (F_N) against Double Bond Conversion (DBC) for formulation contained the reference system/ acetal-based monomer and NAM (1:4 DB-ratio), and 1 mol% PI. D3MA in orange (—), VMA in dark blue (—), DMMA in yellow (—), T5MA in dark green (—) and MB5MA in dark red (—). (Gray dashed line indicates body temperature).

Dynamic Mechanical Thermal Analysis (DMTA).

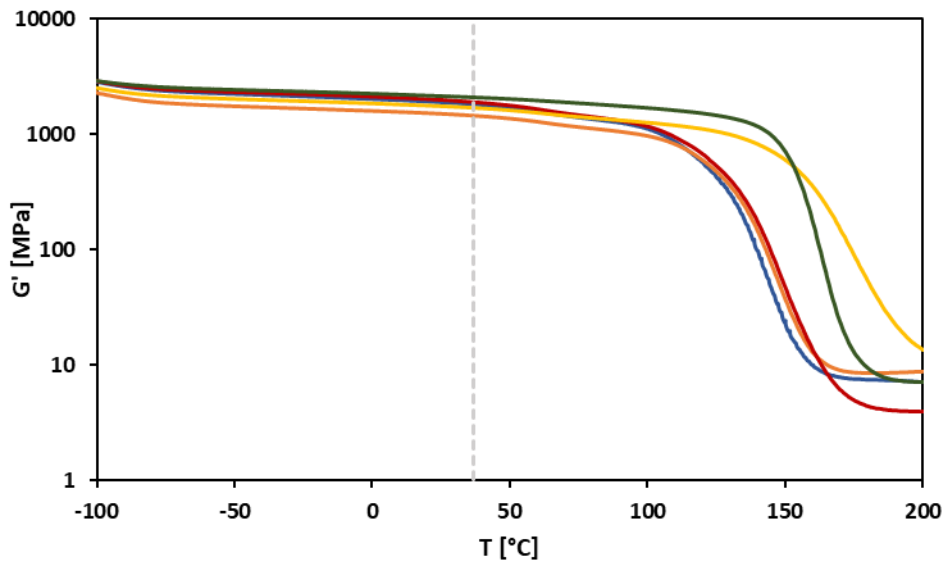
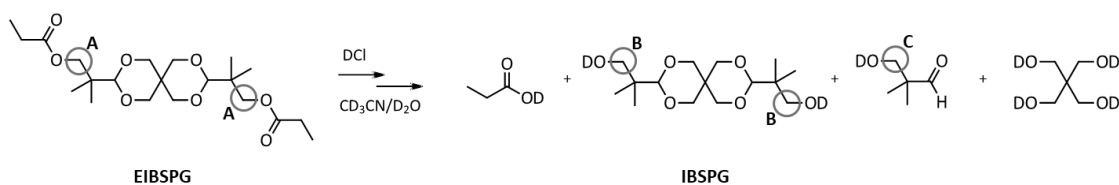


Figure S. 4: Results of DMTA measurements: Storage modulus G' for photopolymerized specimen; formulation contained the reference system/ acetal-based monomer and NAM (1:4 DB-ratio), and 1 mol% PI. D3MA in orange (—), VMA in dark blue (—), DMMA in yellow (—), T5MA in dark green (—) and MB5MA in dark red (—). (Gray dashed line indicates body temperature).

Degradation Experiments

Degradation study of the reference system, containing the spiroacetal and ester moiety were conducted via $^1\text{H-NMR}$ spectroscopy and the experiment was performed at room temperature. The sample was dissolved in a $\text{D}_2\text{O}/\text{CD}_3\text{CN}$ mixture (0.7 mL) and by addition of 0.5 μL DCl an acidic environment is created, which is equivalent to a pH value of 2.1. Increase or decrease of characteristic signals are followed over time and the residual mol% of the acetals are drawn against the time.



Scheme S. 1: Degradation of EIBSPG under acidic conditions.

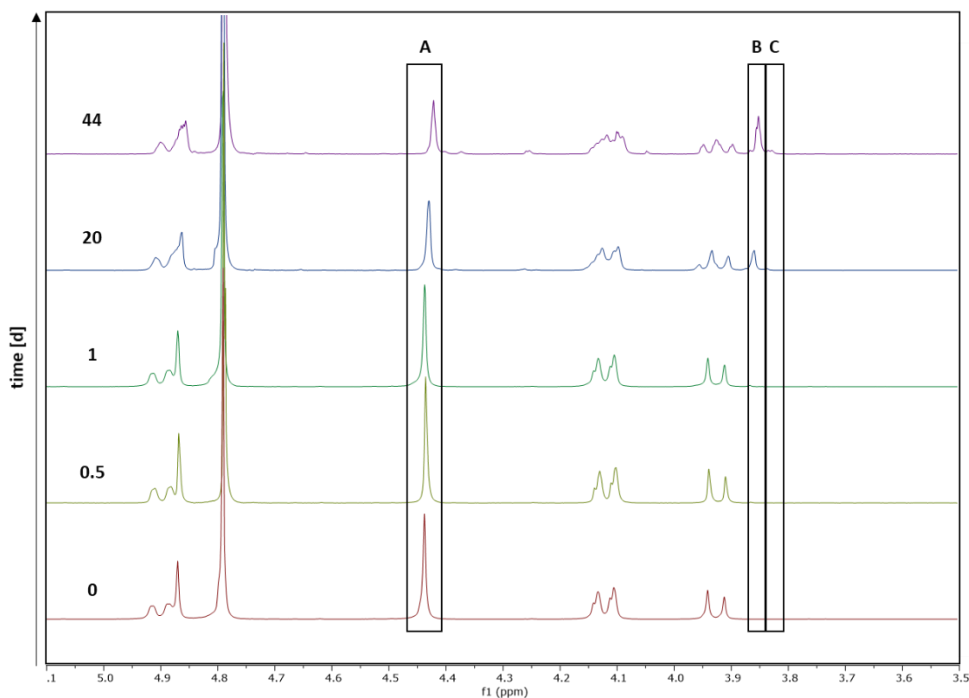


Figure S. 5: $^1\text{H-NMR}$ spectrum ($\text{CD}_3\text{CN}:\text{D}_2\text{O}$ (1:1) + 0.5 μl DCl (38 wt% DCl in D_2O), pH-equivalent of 2.1) of EIBSPG under acidic conditions during a period of 44 days; Time t_0 (0 d) bottom spectrum and t_5 (44 d) top spectrum. A: standardized CH_2 -signal of EIBSPG; B: referenced CH_2 -signal of IBSPG; C: referenced CH_2 -signal of 3-hydroxy-2,2-dimethylpropanol.

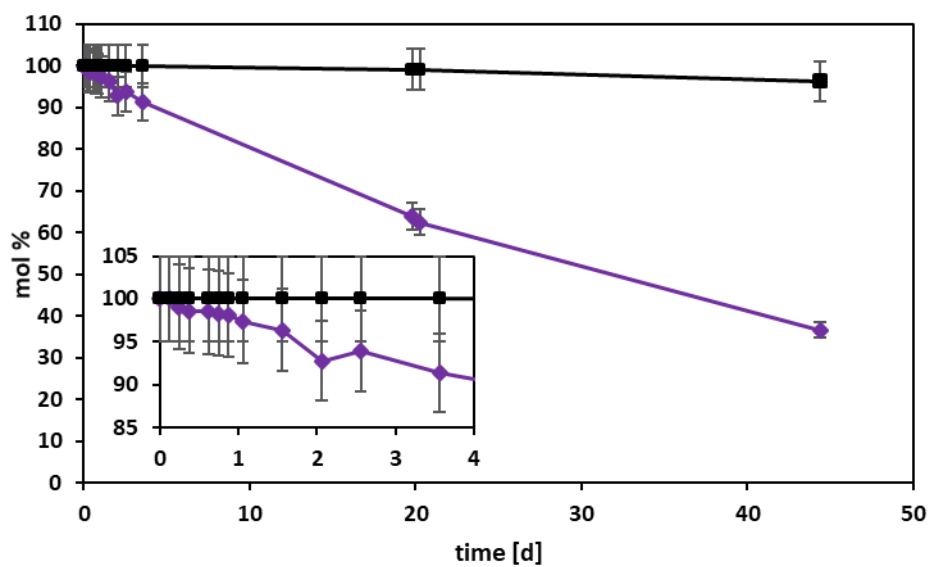
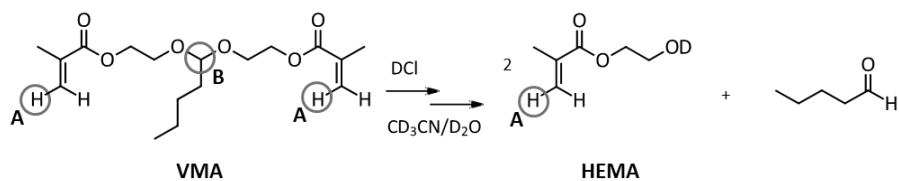


Figure S. 6: Degradation process of the spiroacetal moiety in black (square ■) and the ester moiety in purple (diamond ◆) under acidic conditions (pH-equivalent of 2.1) during a period of 45 days. (For a better visibility, the symbols were connected with straight lines.)



Scheme S. 2: Degradation of VMA under acidic conditions.

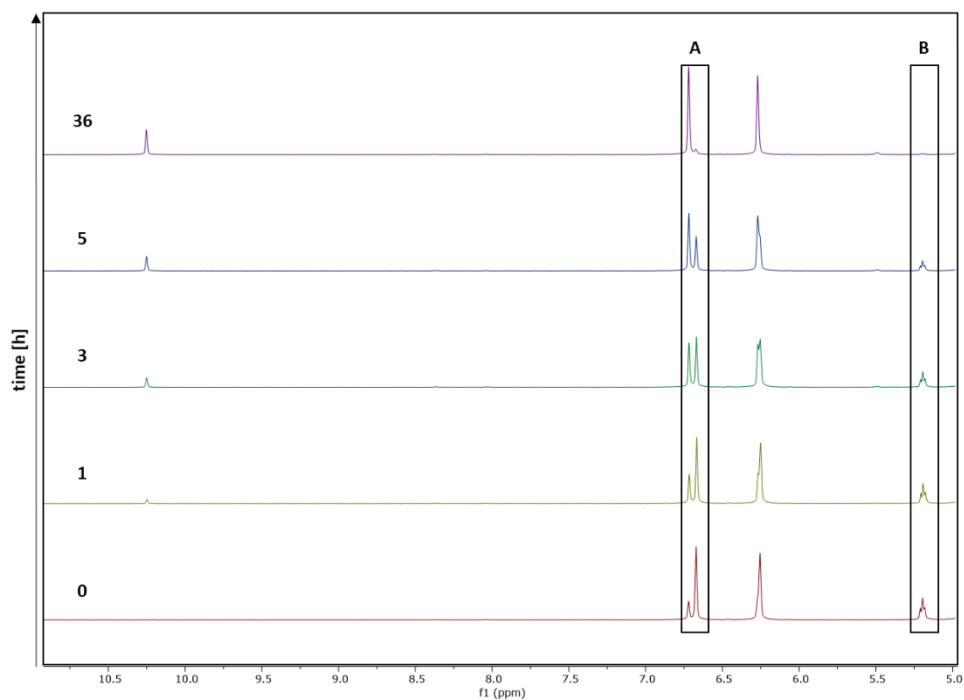
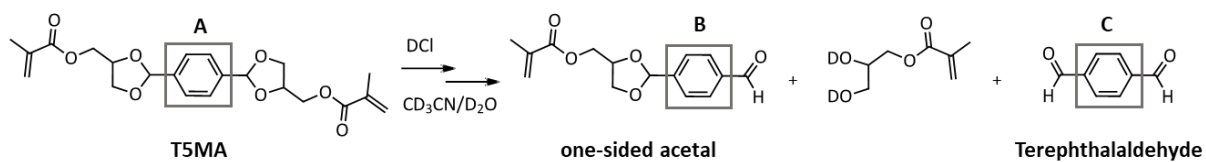


Figure S. 7: ¹H-NMR spectrum ($\text{CD}_3\text{CN}:\text{D}_2\text{O}$ (1:1) + $0.5 \mu\text{l}$ DCl (38 wt% DCl in D_2O), pH-equivalent of 2.1) of VMA under acidic conditions during a period of 36 hours; Time t_0 (0 h, bottom) and t_5 (36 h, top). A: standardized CH-H-signal of the double bond of VMA; B: referenced CH-(O)₂-signal of VMA.



Scheme S. 3: Degradation of T5MA under acidic conditions.

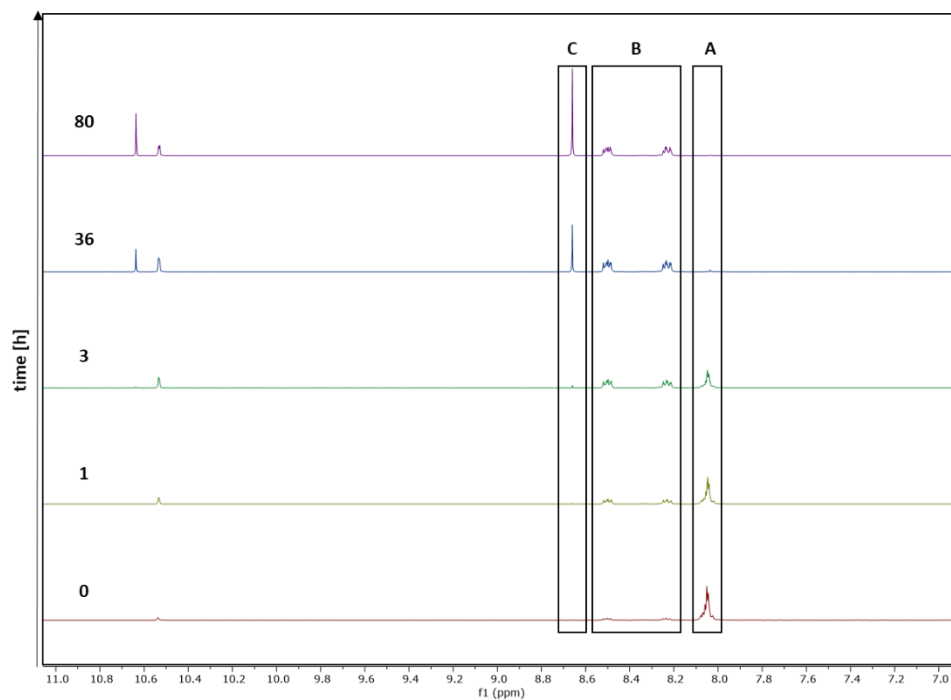
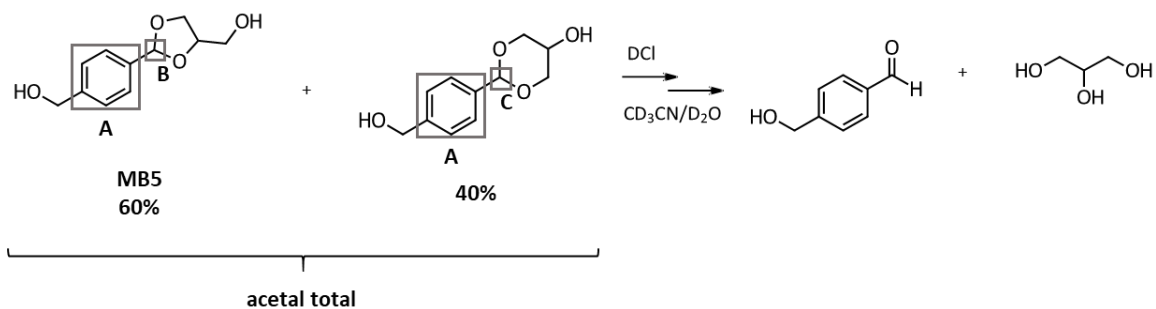


Figure S. 8: ¹H-NMR spectrum ($\text{CD}_3\text{CN}:\text{D}_2\text{O}$ (1:1) + 0.5 μl DCl (38 wt% DCl in D_2O), pH-equivalent of 2.1) of T5MA under acidic conditions during a period of 80 hours; Time t_0 (0 h, bottom) and t_5 (80 h, top). A: standardized Ar-H-signals T5MA; B: referenced Ar-H-signals of the one-side-degraded molecule; C: referenced Ar-H of the two-side-degraded terephthalaldehyde.



Scheme S. 4: Degradation of the diol under acidic conditions (some of the protons are exchanged with deuterium).

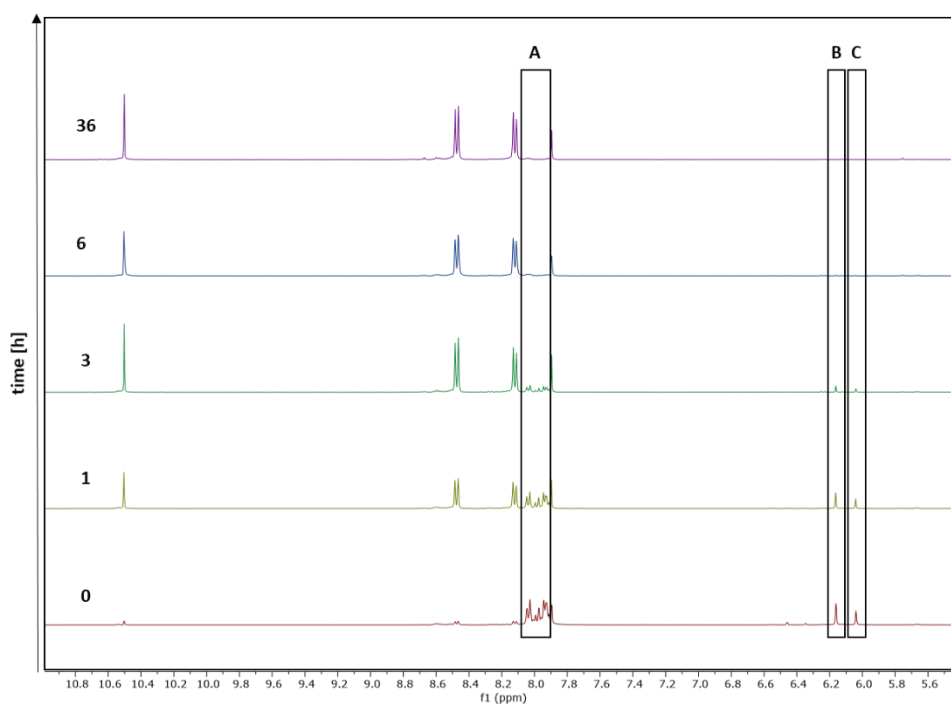


Figure S. 9: $^1\text{H-NMR}$ spectrum ($\text{CD}_3\text{CN:D}_2\text{O}$ (1:1) + $0.5 \mu\text{l DCl}$ (38 wt% DCl in D_2O), pH-equivalent of 2.1) of the diol under acidic conditions during a period of 36 hours; Time t_0 (0 h, bottom) and t_5 (36 h, top).

A: standardized Ar-H-signals of the diols; B: referenced to -CH(O)-signals of the 5-membered ring; C: referenced -CH(O)-signals of the 6-membered ring.