Supplementary information

Simultaneous formation of polyhydroxyurethanes and multicomponent semi-IPN hydrogels

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# Synthesis and characterization of small molecules and monomers

## Synthesis of the organo-catalyst {1-[3,5-bis(trifluoromethyl)phenyl]-3-cyclohexylthiourea} (TU)

|  |  |
| --- | --- |
|  | The catalyst TU was synthesized following a reported procedure [1] with slight modifications. To a solution of 3,5‑di(trifluoromethyl)phenyl isothiocyanate (600 mg, 2.21 mmol) in tetrahydrofuran (THF, 10 mL), cyclohexylamine  |

(278 μL, 2.43 mmol) was added and the solution was stirred at room temperature (r.t.) for 4 hours. The solvents were evaporated, and the resulting residue was purified by flash column chromatography on silica gel [*tert*‑butyl methyl ether (*t*BME)-hexane 1:4 → *t*BME-hexane 1:2] to give the title compound (801 mg, 2.17 mmol, 98%) as a white solid.

IR (ν cm-1) 3294, 3163 (N-H), 3030, 2935, 2861 (C-H), 1556 (C=S), 1526, 1468 (arom.).

1H-NMR (300 MHz, CDCl3) δ (ppm) 8.13 (bs, 1H, Ph-NH-), 7.76 (s, 2H, H-2’, H-6’), 7.71 (s, 1H, H-4’), 6.07 (bs, 1H, -NH-cyclohexyl, 4.19 (bs, 1H, H-1), 2.07 (dd, H-2a, H-6a, 2*J*2a,2b = 2*J*6a,6b = 12.4 Hz, *J*2a,3a = *J*6a,5a 3.3 Hz), 1.70-1.10 (m, 8H, H-2b, H-3, H-4, H-5, H-6b). 13C-NMR (75 MHz, CDCl3) δ (ppm) 179.3 (C=S), 138.9 (C-1’), 124.6 (C-2’, C-6’), 123.9 (C-3’, C-5’), 120.9 (-CF3), 119.4 (C-4’), 54.0 (C-1), 32.4 (C-2, C-6), 35.3 (C-4), 24.6 (C-3, C-5).

## Synthesis of bis(cylic carbonate) monomer A (MA) from 1‑thioglycerol

The synthesis of MA was carried out by the three-step procedure displayed in Scheme 2 starting from 1-thioglycerol.

### Synthesis of 3-(prop-2-yn-1-ylthio)-propane-1,2-diol (**1**)

|  |  |
| --- | --- |
|  | A solution of 1-thioglycerol (0.87 mL, 10 mmol) and TEA (1.5 mL, 11 mmol) in acetonitrile (MeCN, 5 mL) was cooled to 0 °C. An 80% w/v solution of propargyl bromide in toluene (1.2 mL, 11 mmol) was added dropwise and the solution was stirred at 25 °C for 5 h. |

The reaction mixture was diluted with dichloromethane (CH2Cl2, 20 mL) and washed with double distilled water (15 mL). The aqueous phase was extracted with ethyl acetate (EtOAc, 20 mL x 3) and the combined organic phases were dried by the addition of anhydrous sodium sulfate, filtrated, and the solvents removed under reduced pressure. The residue was purified by flash column chromatography (*t*BME‑hexane 1:2) to give the title compound (**1**) as an uncolored oil (1.32 g, 90%).

IR: ν (cm-1) 3370 (OH), 3284 (≡C-H), 2175 (C≡C).

1H-NMR (CDCl3, 500 MHz) δ (ppm) 3.93-3.89 (m, 1H, H-2), 3.79-3.75 (m, 1H, H‑1a), 3.62-3.57 (m, 1H, H‑1b), 3.33 (dd, 1H, H-4a, *J4a,6* = 2.7 Hz, 2*J4a,4b* = 17.0 Hz), 3.28 (dd, 1H, H-4b, *J*4b,6 = 2.5 Hz), 2.91 (dd, 1H, H-3a, *J3a,2* = 4.0 Hz, 2*J3a,3b* = 13.9 Hz), 2.78 (dd, 1H, H-3b, *J3b,2* = 8.0 Hz), 2.28 (t, 1H, H-6), 2.12, 1.65 (2 bs, 2H, OH). 13C-NMR (CDCl3, 125 MHz) δ (ppm) 79.7 (C‑5), 71.6 (C‑6), 69.9 (C-2), 65.3 (C-1), 35.4 (C-3), 19.7 (C-4).

FTMS+cESIFullms: Calculated molecular weight for C6H10O2NaS (M + Na)+ 169.0294; experimental molecular weight: 169.0291.

### Synthesis of 4-[(prop-2-yn-1-ylthio)methyl]-1,3-dioxolan-2-one (**2**)

|  |  |
| --- | --- |
|   | A solution of bis(trichloromethyl) carbonate (0.81 g, 2.74 mmol) in dichloromethane (CH2Cl2, 6 mL) was added dropwise to a cooled solution (-55 °C) of pyridine (2.4 mL, 32.8 mmol) and the diol **1** (0.4 g, 2.74 mmol) in CH2Cl2 (8 mL).  |

Once the addition was complete, the reaction was then allowed to warm to room temperature and stirred overnight. The reaction mixture was quenched with saturated aqueous ammonium chloride (20 mL) and the aqueous phase was extracted with CH2Cl2 (20 mL x 3). The combined organic extracts were washed with 1M HCl, saturated aqueous NaHCO3, brine, distilled water and then dried (Na2SO4), filtered and concentrated under vacuum. The residue was purified by column chromatography (*t*BME-Hex 1:1) to give the title compound (**2**) as a colored oil (0.45 g, 96%).

IR: ν (cm-1) 3275 (≡C-H), 2919 (aliphatic C-H), 2359 (C≡C), 1788 (C=O st).

1H-NMR (CDCl3, 500 MHz) δ (ppm) 5.00-4.94 (m, 1H, H-2), 4.59 (t, 1H, H-1a, 2*J1a,1b* = *J1a,2* = 8.4 Hz), 4.32 (dd, 1H, H-1b, *J1b,2* = 7.0 Hz), 3.35 (d, 2H, H-4, *J4,6* = 2.7 Hz), 3.12 (dd, 1H, H­3a, *J3a,2* = 4.9 Hz, 2*J3a,3b* = 14.5 Hz), 2.99 (dd, 1H, H-3b, *J3b,2* = 7.0 Hz ), 2.33 (t, 1H, H-6). 13C-NMR (CDCl3, 125 MHz) δ (ppm) 154.4 (C=O), 79.0 (C­5), 75.3 (C-2), 72.5 (C-6), 68.6 (C-1), 33.9 (C-3), 20.2 (C-4).

FTMS+cESIFullms: Calculated molecular weight for C7H8O3NaS (M + Na)+ 195.0086; experimental molecular weight: 195.0084.

### Synthesis of bis(cylic carbonate) Monomer A

|  |  |
| --- | --- |
|   | To a solution of the propargyl cyclic carbonate **2** (402 mg, 2.33 mmol) in *tert*‑butanol-water 2:1 (90 mL), the freshly prepared diazide **3** ([23], |

217 mg, 1.06 mmol), sodium ascorbate (46 mg, 0.233 mmol) and cupper (II) sulfate (CuSO4, 8.5 mg, 0.053 mmol) were added and the solution was stirred at r.t. for 19 h. The solvent was evaporated, and the resulting residue was purified by flash column chromatography on silica gel (CH2Cl2 → CH2Cl2-MeOH 10:1, 0.5% TEA) to give monomer A (271 mg, 0.495 mmol, 46.7%) as a colorless oil. The azido-cyclic carbonate derived from the functionalization of one of the propargyl unit was also isolated (161 mg, 0.429 mmol, 40.5%).

IR (ν cm-1) 3137 (C-H triazole), 2922 (aliphatic C-H), 1790 (C=O st cyclic carbonate).

1H-NMR (500 MHz, CDCl3) δ (ppm) 7.65 (s, 2H, H-6), 4.92-4.83 (m, 2H, H-2), 4.66 (t, 4H, *J*7,8 = 6.5 Hz, H-7), 4.53 (t, 2H, 2*J*1a,1b = *J*1a,2 = 8.5 Hz, H-1a), 4.21 (dd, 2H, *J*1b,2 = 6.5 Hz, H-1b), 3.92 (d, 2H, 2*J*4a,4b = 14.5 Hz, H-4a), 3.89 (d, 2H, H-4b), 3.21 (t, 4H, H-8), 2.95 (dd, 2H, *J*3a,2 = 5.0 Hz, 2*J*3a,3b = 14.0 Hz, H-3a), 2.87 (dd, 2H, *J*3b,2 = 6.5 Hz, H-3b). 13C-NMR (125 MHz, CDCl3) δ (ppm) 154.6 (C=O), 144.9 (C-5), 123.1 (C-6), 75.5 (C-2), 68.6 (C-1), 48.7 (C-7), 37.9 (C-8), 34.1 (C-3), 26.7 (C-4).

HRESIMS *m/z* found 571.0531, calc. for C18H24N6O6NaS4 [M+Na]+: 571.0532.

## Synthesis of bis(cylic carbonate) Monomer E

|  |  |
| --- | --- |
|  | 4-Vinyl-1,3-dioxolan-2-one (or vinyl-ethylcarbonate, VEC, 0.96 mL, 10 mmol) and 2,3-dimercapto-1-propanol (or 1,2‑dithio-glycerol, 0.40 mL, 4 mmol) were dissolved in 5 mL of methanol.  |

The solution was degassed for 10 minutes. Then, 2,2-dimethoxy-2-phenylacetophenone (DMPA, 205 mg, 0.8 mmol) was added and the solution was exposed for 10 minutes at UV radiation (365 nm, 180 W) and the reaction solution was stirred overnight at r.t. The solvent was evaporated, and the crude product was purified by column chromatography on silica gel (*t*BME → *t*BME‑MeOH 5:1) to give monomer E as a pure, slightly colored oil (1.254 g, 3.56 mmol, 89%).

IR (ν cm-1) 3479 (OH), 2922 (aliphatic C-H), 1776 (C=O).

1H-NMR (300 MHz, CDCl3) δ (ppm) 4.99-4.85 (m, 2H, H-2, H-2’), 4.61 (t, 2H, *J1a,2* = 8.6 Hz, H-1a, H-1’a), 4.20-4.09 (m, 2H, H-1b, H-1’b), 3.85-3.70 (m, 2H, H-7), 3.50 (bs, 1H, O-H), 2.99-2.88 (m, 1H, H-5), 2.88-2.63 (m, 6H, H-4, H-4’ and H-6), 2.22-2.06 (m, 2H, H-3a, H-3’a), 2.05-1.90 (m, 2H, H-3b, H-3’b). 13C-NMR (75 MHz, CDCl3) δ (ppm) 154.7 (C=O), 75.4 (C-2, C-2’), 69.2 (C-1, C-1’), 63.4 (C-7), 49.0 (C-5), 34.5 (C-3, C-3’), 28.1 and 26.4 (C-4, C-4’ and C-6).

FTMS+cESIFullms: Calculated molecular weight for C13H20O7NaS2 (M + Na)+: 375.0543; experimental molecular weight: 375.0537.

# Tables of Polymerization conditions tested for the formation of PHU

**Table S1**. Polymerization conditions tested for the preparation of PHU‑ADETA (aminolysis of MA with DETA) and weight average molecular weights ($\overbar{M\_{w}}$) achieved.

| **Entries** | **Samples****PHU-ADETA** | **[Monomer]** | **Solvent** | **Temp. (°C)** | **Catalyst** | ***Mw*(a)****(g/mol)** |
| --- | --- | --- | --- | --- | --- | --- |
| **1** | **ADETA-1** | 165 mmol/L | TFE | 25 | -- | -- |
| **2** | **ADETA-2** | TFE | 50 | -- | 3,700 |
| **3** | **ADETA-3** | DMSO | 25 | -- | -- |
| **4** | **ADETA-4** | DMSO | 50 | -- | 3,400 |
| **5** | **ADETA-5** | TFE | 25 | TU | 7,700 |
| **6** | **ADETA-6** | TFE | 50 | TU | 6,800 |
| **7** | **ADETA-7** | DMSO | 25 | TU | 6,500 |
| **8** | **ADETA-8** | DMSO | 50 | TU | 5,400 |
| **9** | **ADETA-9** | TFE | 25 | DBU | 13,800 |
| **10** | **ADETA-10** | TFE | 50 | DBU | 9,600 |
| **11** | **ADETA-11** | DMSO | 25 | DBU | 14,300 |
| **12** | **ADETA-12** | DMSO | 50 | DBU | 8,700 |
| **13** | **ADETA-13** | 1.8 mol/L | TFE | 25 | TU | 16,400 |
| **14** | **ADETA-14** | TFE | 50 | TU | 8,500 |
| **15** | **ADETA-15** | DMSO | 25 | TU | 10,800 |
| **16** | **ADETA-16** | DMSO | 50 | TU | 7,900 |
| **17** | **ADETA-17** | TFE | 25 | DBU | 8,600 |
| **18** | **ADETA-18** | TFE | 50 | DBU | 9,000 |
| **19** | **ADETA-19** | DMSO | 25 | DBU | 11,200 |
| **20** | **ADETA-20** | DMSO | 50 | DBU | 14,700 |
| (a) Weight average molecular weight ($\overbar{M\_{w}}$) calculated by gel permeation chromatography. DBU: 1,8-Diazabicyclo[5.4.0]undec-7-ene; DMSO: dimethylsulfoxide; TFE: 2,2,2-trifluoroethanol; TU: *N′*-[3,5-bis(trifluoromethyl)phenyl]-*N*-cyclo-hexylthiourea. |

**Table S2**. Polymerization conditions tested for the preparation of PHU-EDETA and PHU‑EHMDA (by reaction of ME with DETA and HMDA, respectively) and weight average molecular weights ($\overbar{M\_{w}}$) achieved.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Entries** | **Samples****PHU-EDETA** | **Diamine** | **Solvent** | **Temp. (°C)** | **Catalyst** | ***Mw*(a)****(g/mol)** |
| **1** | **EDETA-1** | DETA | DMSO | 50 | TU | 21,800 |
| **2** | **EDETA-2** | DMSO | 50 | DBU | 13,800 |
| **3** | **EDETA-3** | EtOH | 25 | TU | 14,500 |
| **4** | **EDETA-4** | EtOH | 50 | TU | 29,600 |
| **5** | **EDETA-5** | EtOH | 50 | DBU | 10,300 |
| **Entries** | **Samples****PHU-EHMDA** | **Diamine** | **Solvent** | **Temp. (°C)** | **Catalyst** | ***Mw*(a)****(g/mol)** |
| **6** | **EHMDA-1** | HMDA | DMSO | 25 | DBU | 20,300 |
| **7** | **EHMDA-2** | DMSO | 50 | DBU | 34,100 |
| **8** | **EHMDA-3** | DMSO | 50 | TU | 18,500 |
| **9** | **EHMDA-4** | EtOH | 50 | TU | 13,600 |
| **10** | **EHMDA-5** | EtOH | 50 | DBU | 13,700 |
| (a) Weight average molecular weight ($\overbar{M\_{w}}$) calculated by gel permeation chromatography. DBU: 1,8-Diazabicyclo[5.4.0]undec-7-ene; DMSO: dimethylsulfoxide; EtOH: ethanol; TU: *N*′-[3,5-bis(trifluoromethyl)phenyl]-*N*-cyclohexylthiourea. |

# References

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