Tunable polymers obtained from Passerini multicomponent reaction derived acrylate monomers

Ansgar Sehlinger, Oliver Kreye, Michael A. R. Meier

Laboratory of Applied Chemistry, Institute of Organic Chemistry, Karlsruhe Institute of Technology (KIT), Fritz-Haber-Weg 6, 76131 Karlsruhe, Germany.

Table of contents
1. Supporting Information .................................................................................................................... 1
   1.1 Isocyanide syntheses ..................................................................................................................... 1
   1.2 Monomer syntheses ....................................................................................................................... 7
   1.3 Free radical polymerization ......................................................................................................... 26
2. UCST measurements ....................................................................................................................... 36
3. References ........................................................................................................................................ 40

1. Supporting Information

1.1 Isocyanide syntheses

1.1.1 Benzyl isocyanide (2d)

\[
\text{Benzyl amine} \xrightarrow{\text{1. n-butyl formate, reflux / 22 h}} \text{Benzyl isocyanide (2d)} \xrightarrow{\text{2. PCC / \text{NE}_3, 0^\circ\text{C} - \text{rt} / 3 h}} \text{58\% (two steps)}
\]
A mixture of benzyllamine (5.00 g, 5.09 mL, 46.7 mmol), n-butylformate (53.6 g, 55.9 mL, 525 mmol) and triethylamine (9 mL) was dissolved in 90 mL xylene and refluxed for 22 hours. Then, the reaction mixture was evaporated under reduced pressure and the residue was recrystallized from hexane to yield N-benzylformamide as a colorless solid (5.77 g, 91.4 %). TLC (ethyl acetate/ MeOH 9:1) \( R_f = 0.67 \); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \( \delta \) (ppm) = 4.40 (d, \( J = 5.9 \) Hz, 2 H, CH\(_2\)), 5.94 (br, 1 H, NH), 7.10-7.34 (m, 5H, 5 Ar-H), 8.17 (s, 1 H, CHO); \( T_m = 60.4 \) °C (hexane).

\( N \)-benzylformamide (5.75 g, 42.6 mmol) was dissolved in 40 mL dichloromethane and 4.3 mL triethylamine (31 mmol) were added. The mixture was cooled down with a NaCl ice bath. Subsequently, POCl\(_3\) (7.18 g, 4.27 mL, 46.8 mmol) was slowly added. Then, the reaction mixture was allowed to warm up at room temperature and stirring was maintained for three hours. Afterwards, cool NaHCO\(_3\) solution (50 mL) was added. The organic layer was separated, washed with brine (2 x 50 mL), dried over Na\(_2\)SO\(_4\) and evaporated under reduced pressure. The residue was purified by flash silica gel column chromatography (n-hexane/ethyl acetate 1:1) to obtain benzyl isocyanide 2d as brown liquid (3.18 g, 64 %). TLC (n-hexane/ethyl acetate 9:1) \( R_f = 0.51 \); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \( \delta \) (ppm) = 4.65 (s, 2 H, CH\(_2\)), 7.30-7.50 (m, 5 H, Ar-H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \( \delta \) (ppm) = 45.48, 45.58, 45.68, 126.67, 128.47, 129.04, 132.40, 157.66, 157.73, 157.80.
1.1.2 Methyl 4-aminobutyrate hydrochloride

4-Aminobutyric acid (GABA, 20.0 g, 194 mmol) was suspended in methanol (300 mL) and cooled down with an ice bath to 0°C. Subsequently, thionyl chloride (71.4 g, 600 mmol, 3.0 eq.) was dropped to the strongly stirred solution. Then, the reaction mixture was allowed to reach room temperature and was stirred for about one day. The clear solution was evaporated to dryness under reduced pressure and the obtained colorless solid washed intensively with diethyl ether (~300 mL). After drying, pure methyl 4-aminobutyrate hydrochloride was obtained as colorless crystals (29.7 g, quant.). $^1$H NMR (CD$_3$OD, 300 MHz) $\delta$ (ppm) = 1.96 (quint., $J$ = 7.4 Hz, 2 H, CH$_2$), 2.50 (t, $J$ = 7.2 Hz, 2 H, CH$_2$CO$_2$Me), 3.00 (t, $J$ = 7.6 Hz, 2 H, CH$_2$NH$_3^+$), 3.69 (s, 3 H, COOCH$_3$); $^{13}$C NMR (CD$_3$OD, 75 MHz) $\delta$ (ppm) = 23.7 (CH$_2$), 31.4 (CH$_2$CO$_2$Me), 40.0 (CH$_2$NH$_3^+$), 52.3 (COOCH$_3$), 174.5 (CO$_2$Me); FAB of C$_9$H$_{12}$NO$_2$ (M$^+$ = 118.3). $T_m$ = 120-121°C (diethyl ether).
1.1.3 Methyl 4-isocyanobutyrate (2e)

Methyl 4-aminobutyrate hydrochloride (20.0 g, 130 mmol) was suspended in trimethyl orthoformate (45 mL) and heated to reflux under stirring. The reaction progress was controlled by TLC (dichloromethane/ methanol 9:1) and after six hours a full conversion was detected. Then the reaction mixture was evaporated to dryness under reduced pressure to obtain methyl 4-(N-formyl)aminobutyrate as colorless oil (18.9 g, quant.). TLC (dichloromethane/ methanol 9:1) $R_f = 0.66$; $^1$H NMR (CDCl$_3$, 300 MHz, mixture of cis/trans-amide bonds, isomer ratio trans : cis 4.4:1) $\delta$ (ppm) = 1.87 (quint., $J = 7.2$ Hz, 2 H, CH$_2$), 2.40 (t, $J = 7.2$ Hz, 2 H, CH$_2$CO$_2$Me), 3.34 (q, $J = 6.8$ Hz, 2 H, CH$_2$NH), 3.68 (s, 3 H, COOC$_3$), 6.67 (br, s, 1 H, NH), 8.03 (d, $J = 11.7$ Hz, 1 H, NHCHO, cis), 8.16 (s, 1 H, NHCHO, trans); FAB of C$_6$H$_{11}$NO$_3$ (M+H$^+$ = 146.4; M+Na$^+$ = 168.0).

The formamide (18.9 g, 130 mmol) was dissolved in dichloromethane (350 mL) and diisopropylamine (39.5 g, 391 mmol, 3.0 eq.) was added. Then the reaction mixture was cooled down with an ice bath to 0°C and subsequently, the solution of phosphorus oxychloride (24.0 g, 156 mmol, 1.2 eq.) in dichloromethane (50 mL) dropped to the strong stirred solution. The mixture was allowed to reach room temperature and after two hours TLC identification (dichloromethane/ methanol 9:1) detected a full conversion. The reaction was quenched by addition of a sodium carbonate solution (20%, 200 mL). After additional thirty minutes dichloromethane (100 mL) and water (100 mL) were added. The organic layer was separated, dried over sodium sulfate and then evaporated to dryness. The crude methyl 4-isocyanobutyrate 2e was purified by flash chromatography (dichloromethane/ methanol 9:1) to obtain pure 2e as slightly yellow liquid (14.9 g, 90%). TLC (dichloromethane/ methanol 9:1) $R_f = 0.87$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ (ppm) = 1.97-2.04 (m, 2 H, CH$_2$), 2.52 (t, $J = 7.0$ Hz, 2 H,
$\text{CH}_2\text{CO}_2\text{Me}$, 3.49-3.53 (m, 2 H, $\text{CH}_2$NC), 3.71 (s, 3 H, COOCH$_3$). $^{13}$C NMR (CDCl$_3$, 75 MHz) $\delta$ (ppm) = 24.1 ($\text{CH}_3$), 30.0 ($\text{CH}_2$CO$_2$Me), 40.7 (triplet, $\text{CH}_2$NC), 51.7 (COOCH$_3$), 156.5 (triplet, –NC) 172.4 (CO$_2$Me); IR (ATR) $\nu$ = 2148.5 (NC), 1731.5 (CO$_2$Me) cm$^{-1}$.
1.2 Monomer syntheses

![Diagram of monomer synthesis]

<table>
<thead>
<tr>
<th>product</th>
<th>$R^1$</th>
<th>$R^2$</th>
<th>solvent</th>
<th>yield [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>$-t$-Bu (2a)</td>
<td>-Ph (3a)</td>
<td>water / DCM</td>
<td>41 / 12</td>
</tr>
<tr>
<td>4b</td>
<td>$-t$-Bu (2a)</td>
<td>-(CH$_2$)$_3$CH$_3$ (3b)</td>
<td>water / DCM</td>
<td>68 / 45</td>
</tr>
<tr>
<td>4c</td>
<td>$-t$-Bu (2a)</td>
<td>-$i$-Pr (3c)</td>
<td>water / DCM</td>
<td>74 / 89</td>
</tr>
<tr>
<td>4d</td>
<td>$-t$-Bu (2a)</td>
<td>-Et (3d)</td>
<td>water / DCM</td>
<td>67 / 77</td>
</tr>
<tr>
<td>4e</td>
<td>$-t$-Bu (2a)</td>
<td>-Me (3e)</td>
<td>DCM</td>
<td>86</td>
</tr>
<tr>
<td>4f</td>
<td>-$c$-Hx (2b)</td>
<td>-Me (3e)</td>
<td>DCM</td>
<td>100</td>
</tr>
<tr>
<td>4g</td>
<td>-(CH$_2$)$_3$CH$_3$ (2c)</td>
<td>-Me (3e)</td>
<td>DCM</td>
<td>100</td>
</tr>
<tr>
<td>4h</td>
<td>-Bn (2d)</td>
<td>-Me (3e)</td>
<td>DCM</td>
<td>74</td>
</tr>
<tr>
<td>4i</td>
<td>-(CH$_2$)$_3$CO$_2$Me (2e)</td>
<td>-Me (3e)</td>
<td>DCM</td>
<td>94</td>
</tr>
</tbody>
</table>

**General procedure for acrylate synthesis via P-3CR:**

Freshly distilled acrylic acid 1 (721 mg, 686 µL, 10.0 mmol), acetaldehyde 3e (440 mg, 560 µL, 10.0 mmol) and 10 mL dichloromethane were mixed in a round bottom flask. Subsequently, the appropriate isocyanide 2a-e (10.0 mmol) was added under stirring. After 24 hours of vigorous stirring at room temperature, the reaction mixture was concentrated under reduced pressure. The residue was either pure (see 4f and 4g) or further purified by silica gel column chromatography ($n$-hexane/ethyl acetate =2:1).

Alternative procedure in deionized water: Freshly distilled acrylic acid 1 (721 mg, 686 µL, 10.0 mmol), the desired aldehyde 3a-d (10.0 mmol) and 20 mL water were mixed together in a round bottom flask. Subsequently, tert-butyl isocyanide 2a (831 mg, 1.13 mL, 10.0 mmol) was added under stirring. After three hours of vigorous stirring at room temperature, the product was precipitating as a colorless solid. Direct filtration and high vacuum drying yielded the pure Passerini product.
1.2.1 2-(tert-Butylamino)-2-oxo-1-phenylethyl acrylate (4a)

The Passerini-3CR of acrylic acid \(\mathbf{1}\) (721 mg, 6.86 µL, 10.0 mmol), benzaldehyde \(\mathbf{3a}\) (1.06 g, 1.01 mL, 10.0 mmol) and tert-butyl isocyanide \(\mathbf{2a}\) (831 mg, 1.13 mL, 10.0 mmol) in water led to the formation of 2-(tert-butylamino)-2-oxo-1-phenylethyl acrylate. Direct Filtration yielded \(\mathbf{4a}\) as a colorless solid (1.06 g, 41%). TLC \(R_f = 0.30\) (n-hexane/ethyl acetate = 4:1); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) (ppm) = 1.36 (s, 9 H, 3 CH\(_3\)), 5.87-6.00 (m, 1 H, NH), 5.94 (dd, \(J = 10.3, 1.1\) Hz, 1 H, CH\(_2\)CHCO), 6.05 (s, 1H, OCH), 6.23 (dd, \(J = 17.3, 10.4\) Hz, 1 H, CH\(_2\)CHCO), 6.51 (dd, \(J = 17.3, 1.1\) Hz, 1 H, CH\(_2\)CHCO), 7.30-7.52 (m, 5 H, 5 Ar-H); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \(\delta\) (ppm) = 28.75, 51.65, 75.78, 127.54, 127.71, 128.83, 132.48, 135.93, 164.46, 167.32; FAB of C\(_{15}\)H\(_{19}\)NO\(_3\) [M+H]\(^+\) calc. 262.1443, found 262.1441; IR (ATR) \(\nu\) = 3288.6, 3070.0, 2974.0, 2548.5, 1724.1, 1653.4, 1552.4, 1497.5, 1453.2, 1403.8, 1362.1, 1323.9, 1290.4, 1255.5, 1223.6, 1175.5, 1127.9, 1054.7, 1024.9, 982.6, 960.9, 932.3, 920.3, 802.4, 745.3, 731.2, 700.4, 683.1, 665.9 cm\(^{-1}\); \(T_m = 111\) °C (water).
1.2.2 1-(tert-Butylamino)-1-oxooctan-2-yl acrylate (4b)

The Passerini-3CR of acrylic acid 1 (721 mg, 686 µL, 10.0 mmol), heptanal 3b (1.14 g, 1.41 mL, 10.0 mmol) and tert-butyl isocyanide 2a (831 mg, 1.13 mL, 10.0 mmol) in water led to the formation of 1-(tert-butylamino)-1-oxooctan-2-yl acrylate. Direct Filtration yielded 4b as a colorless solid (1.82 g, 68 %). TLC \( R_f = 0.42 \) \( (n\)-hexane/ethyl acetate = 4:1); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \( \delta \) (ppm) = 0.83 (t, \( J = 6.2 \) Hz, 3 H, CH\(_3\)), 1.15-1.40 (m, 8 H, 4 CH\(_2\)), 1.31 (s, 9 H, 3 CH\(_3\)), 1.68-1.93 (m, 2 H, CHCH\(_2\)), 5.09 (t, \( J = 5.8 \) Hz, 1 H, OCHCO), 5.82 (br, 1 H, NH), 5.93 (dd, \( J = 10.4 \), 1.1 Hz, 1 H, CH\(_2\)CHCO), 6.19 (dd, \( J = 17.3 \), 10.4 Hz, 1 H, CH\(_2\)CHCO), 6.48 (dd, \( J = 17.3 \), 1.1 Hz, 1 H, CH\(_3\)CHCO); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \( \delta \) (ppm) = 14.09, 22.58, 24.68, 28.72, 28.97, 31.65, 31.89, 51.29, 74.51, 127.88, 132.05, 164.88, 168.95; FAB of C\(_{15}\)H\(_{27}\)NO\(_3\) (M+H\(^{+}\) = 270.4); HRMS (FAB) of C\(_{15}\)H\(_{27}\)NO\(_3\) [M+H\(^{+}\)]: calc. 270.2069, found 270.2067; IR (ATR) \( \nu = 3307.3 \), 2957.0, 2926.4, 2858.6, 1728.0, 1659.1, 1620.2, 1552.8, 1454.6, 1402.8, 1363.6, 1260.2, 1220.9, 1187.6, 1120.0, 1076.5, 1055.6, 989.7, 963.3, 932.5, 813.4, 724.9, 648.8, 481.5 cm\(^{-1}\); \( T_m = 54 ^\circ \text{C} \) (water).
1H-NMR (CDCl₃, 300 MHz)

13C-NMR (CDCl₃, 75 MHz)
1.2.3 1-(tert-Butylamino)-3-methyl-1-oxobutan-2-yl acrylate (4c)

The Passerini-3CR of acrylic acid 1 (721 mg, 686 µL, 10.0 mmol), isobutyraldehyde 3c (721 mg, 913 µL, 10.0 mmol) and tert-butyl isocyanide 2a (831 mg, 1.13 mL, 10.0 mmol) in water led to the formation of 1-(tert-butylamino)-3-methyl-1-oxobutan-2-yl acrylate. Direct Filtration yielded 4c as a colorless solid (1.69 g, 74%). TLC (n-hexane/ethyl acetate = 4:1) \( R_f = 0.49 \); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \( \delta \) (ppm) = 0.94 (d, J = 6.9 Hz, 6 H, 2 CH\(_3\)), 1.34 (s, 9 H, 3 CH\(_3\)), 2.25-2.40 (m, 1 H, CH(CH\(_3\))\(_2\)), 5.02 (d, J = 4.3 Hz, 1 H, OCHCO), 5.75 (br, 1 H, NH), 5.94 (dd, J = 10.4, 1.2 Hz 1 H, CH\(_2\)CHCO), 6.20 (dd, J = 17.3, 10.4 Hz, 1 H, CH\(_2\)CHCO), 6.49 (dd, J = 17.3, 1.2 Hz, 1 H, CH\(_3\)CHCO); \(^13\)C NMR (CDCl\(_3\), 75 MHz): \( \delta \) (ppm) = 16.92, 18.83, 28.74, 30.67, 51.35, 78.40, 127.84, 132.10, 164.98, 168.35; FAB of C\(_{12}\)H\(_{21}\)NO\(_3\) (M+H\(^+\) = 228.1); HRMS (FAB) of C\(_{12}\)H\(_{21}\)NO\(_3\) [M+H]\(^+\) calc. 228.1600, found 213.1601; IR (ATR) \( \nu \) = 3273.1, 3086.3, 2966.7, 2934.1, 1720.0, 1656.0, 1560.1, 1455.4, 1406.6, 1390.4, 1363.8, 1294.3, 1266.6, 1224.5, 1193.4, 1126.4, 1110.7, 1059.6, 986.3, 972.3, 941.3, 838.0, 809.8, 757.9, 713.6, 663.3, 582.5, 477.5, 432.0, 408.3 cm\(^{-1}\); \( T_m \) = 87 °C (water).
1.2.4 1-(tert-Butylamino)-1-oxobutan-2-yl acrylate (4d)

The Passerini-3CR of acrylic acid 1 (721 mg, 686 μL, 10.0 mmol), propionaldehyde 3d (581 mg, 717 μL, 10.0 mmol) and tert-butyl isocyanide 2a (831 mg, 1.13 mL, 10.0 mmol) in water led to the formation of 1-(tert-butylamino)-1-oxobutan-2-yl acrylate. Direct Filtration yielded 4d as a colorless solid (1.43 g, 67 %). TLC (n-hexane/ethyl acetate = 4:1) Rf = 0.35; 1H NMR (CDCl3, 300 MHz): δ (ppm) = 0.92 (t, J = 7.5 Hz, 3 H, CH3CH2), 1.35 (s, 9 H, 3 CH3), 1.83-1.97 (m, 2 H, CH2), 5.10 (t, J = 5.6 Hz, 1 H, OCHCO), 5.84 (br, 1 H, NH), 5.93 (dd, J = 10.4, 1.2 Hz 1 H, CH2CHCO), 6.19 (dd, J = 17.3, 10.4 Hz, 1 H, CH2CHCO), 6.48 (dd, J = 17.3, 1.2 Hz, 1 H, CH2CHCO); 13C NMR (CDCl3, 75 MHz): δ (ppm) = 8.92, 25.05, 28.70, 51.30, 51.38, 127.84, 127.94, 131.54, 132.04, 164.82, 168.53, 168.72, 169.40; FAB of C11H19NO3 (M+ = 213.3); HRMS (FAB) of C11H19NO3 [M]+ calc. 213.1365, found 213.1364; IR (ATR) ν = 3306.9, 3080.3, 2971.7, 2938.0, 1723.2, 1695.5, 1635.5, 1551.2, 1454.9, 1399.5, 1363.0, 1295.9, 1268.8, 1243.9, 1225.0, 1191.4, 1132.8, 1107.2, 1091.2, 1054.9, 989.1, 967.3, 940.2, 905.0, 812.2, 756.0, 675.4, 642.5, 502.5, 477.5, 457.8, 406.6 cm⁻¹; Tm = 92 °C (water).
$^1$H-NMR (CDCl$_3$, 300 MHz)

$^{13}$C-NMR (CDCl$_3$, 75 MHz)
1.2.5 1-(tert-Butylamino)-1-oxopropan-2-yl acrylate (4e)

The Passerini 3-CR of acrylic acid 1 (721 mg, 686 µL, 10.0 mmol), acetaldehyde 3e (441 mg, 10.0 mmol) and tert-butyl isocyanide 2a (831 mg, 1.13 mL, 10.0 mmol) dichloromethane led to the formation of 1-(tert-butylamino)-1-oxopropan-2-yl acrylate. After purification by column chromatography (n-hexane/ethyl acetate 2:1), 4e was obtained as colorless solid (1.71 g, 86 %). TLC \( R_f = 0.45 \) (n-hexane/ethyl acetate 2:1); \(^1\)H NMR (CDCl\(_3\), 300 MHz): \( \delta \) (ppm) = 1.35 (s, 9 H, 3 CH\(_3\)), 1.47 (d, J = 6.8 Hz, 3 H, CH\(_3\)), 5.16 (q, J = 6.8 Hz, 1 H, OCHCO), 5.90 (br, 1 H, NH), 5.93 (dd, J = 10.4, 1.0 Hz, 1 H, CH\(_2\)CHCO), 6.17 (dd, J = 17.3, 10.4 Hz, 1 H, CH\(_2\)CHCO), 6.48 (dd, J = 17.3, 1.0 Hz, 1 H, CH\(_2\)CHCO); \(^{13}\)C NMR (CDCl\(_3\), 75 MHz): \( \delta \) (ppm) = 17.88, 28.73, 51.26, 71.06, 127.90, 132.13, 132.13, 164.72, 169.48; EI of C\(_{10}\)H\(_{17}\)NO\(_3\) (M\(^+\) = 199.1); HRMS (EI) of C\(_{10}\)H\(_{17}\)NO\(_3\) [M\(^+\)] calc. 199.1208, found 199.1207; IR (ATR) \( \nu \) = 3287.3, 3078.2, 2969.1, 1730.5, 1657.4, 1551.2, 1480.2, 1453.6, 1405.1, 1360.1, 1309.3, 1283.8, 1263.5, 1224.8, 1192.8, 1138.6, 1099.4, 1052.2, 1033.7, 985.7, 970.2, 929.2, 901.2, 875.7, 803.6, 702.2, 652.0, 479.2, 453.6, cm\(^{-1}\); \( T_m \) = 74 °C (n-hexane/ethyl acetate).
1H-NMR (CDCl$_3$, 300 MHz)

13C-NMR (CDCl$_3$, 75 MHz)
1.2.6 1-(Cyclohexylamino)-1-oxopropan-2-yl acrylate (4f)

The Passerini 3-CR of acrylic acid 1 (721 mg, 686 µL, 10.0 mmol), acetaldehyde 3e (441 mg, 10.0 mmol) and cyclohexyl isocyanide 2b (1.09 g, 1.24 mL, 10.0 mmol) in dichloromethane led to the formation of 1-(cyclohexylamino)-1-oxopropan-2-yl acrylate. After drying in high vacuum, 4f was obtained as slightly yellow solid (2.24 g, quant.). TLC $R_f = 0.48$ ($n$-hexane/ethyl acetate = 2:1); $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ (ppm) = 0.99-1.98 (m, 10 H, 5 CH$_2$), 1.48 (d, J = 6.8 Hz, 3 H, CH$_3$), 3.65-3.84 (m, 1 H, NCH), 5.23 (q, J = 6.8 Hz, 1 H, OCHCO), 5.90-6.04 (m, 1H, NH), 5.91 (dd, J = 10.4, 1.3 Hz, 1 H, CH$_2$CHCO), 6.17 (dd, J = 17.3, 10.4 Hz, 1 H, CH$_2$CHCO), 6.47 (dd, J = 17.3, 1.3 Hz, 1 H, CH$_2$CHCO); $^{13}$C NMR (CDCl$_3$, 75 MHz): $\delta$ (ppm) = 17.99, 24.83, 25.55, 33.04, 48.00, 70.86, 127.84, 132.22, 164.73, 169.31; FAB of C$_{12}$H$_{19}$NO$_3$ (M+H$^+$ = 226.0); HRMS (FAB) of C$_{12}$H$_{19}$NO$_3$ [M+H]$^+$ calc. 226.1443, found 226.1441; IR (ATR) $\nu = 3277.7$, 3093.7, 2931.7, 2852.8, 1725.0, 1656.2, 1560.1, 1449.3, 1400.4, 1289.9, 1271.3, 1251.5, 1190.9, 1140.8, 1095.0, 1037.1, 989.8, 968.8, 891.4, 862.3, 811.1, 671.3, 437.6, 401.6 cm$^{-1}$; $T_m = 61^\circ$C (dichloromethane).
1.2.7 1-Oxo-1-(pentylamino)propan-2-yl acrylate (4g)

![Chemical structure of 1-Oxo-1-(pentylamino)propan-2-yl acrylate](attachment:structure.png)

The Passerini 3-CR of acrylic acid 1 (721 mg, 6.86 µL, 10.0 mmol), acetaldehyde 3e (441 mg, 10.0 mmol) and 1-pentyl isocyanide 2c (972 mg, 1.26 mL, 10.0 mmol) in dichloromethane led to the formation of 1-oxo-1-(pentylamino)propan-2-yl acrylate. After drying in high vacuum, 4g was obtained as clear oily product (2.12 g, quant.). TLC Rf = 0.44 (n-hexane/ethyl acetate = 2:1); ¹H NMR (CDCl₃, 300 MHz): δ (ppm) = 0.89 (t, J = 6.7 Hz, 3 H, CH₃), 1.19-1.39 (m, 4H, 2 CH₂), 1.43-1.57 (m, 2H, CH₂), 1.50 (d, J = 6.8 Hz, 3 H, CH₃), 3.19-3.32 (m, 2 H, NCH₂), 5.29 (q, J = 6.8 Hz, 1 H, OCHCO), 5.93 (dd, J = 10.2, 0.8 Hz, 1 H, CH₂CHCO), 6.02-6.14 (m, 1H, NH), 6.18 (dd, J = 17.3, 10.4 Hz, 1 H, CH₂CHCO), 6.49 (dd, J = 17.3, 0.9 Hz, 1 H, CH₂CHCO); ¹³C NMR (CDCl₃, 75 MHz): δ (ppm) = 13.98, 17.93, 22.32, 28.98, 29.19, 39.27, 70.76, 127.76, 132.18, 164.72, 170.20; EI of C₁₁H₁₉NO₃ (M⁺ = 213.2); HRMS (EI) of C₁₁H₁₉NO₃ [M⁺]⁺ calc. 213.1365, found 213.1363; IR (KBr) ν = 3303.6, 3098.3, 2985.0, 2933.6, 2872.4, 1731.6, 1661.4, 1543.1, 1456.5, 1406.7, 1374.1, 1293.6, 1260.5, 1189.2, 1145.3, 1096.0, 1041.5, 984.0, 895.0, 809.6, 675.5 cm⁻¹.

20
1.2.8 1-(Benzylamino)-1-oxopropan-2-yl acrylate (4h)

The Passerini 3-CR of acrylic acid 1 (721 mg, 686 μL, 10.0 mmol), acetaldehyde 3e (441 mg, 10.0 mmol) and benzyl isocyanide 2d (1.17 g, 1.22 mL, 10.0 mmol) in dichloromethane led to the formation of 1-(benzylamino)-1-oxopropan-2-yl acrylate. After purification by column chromatography (n-hexane/ethyl acetate 2:1), 4h was obtained as a colorless solid (1.73 g, 74 %). TLC $R_f = 0.24$ (n-hexane/ethyl acetate = 2:1); $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ (ppm) = 1.55 (d, J = 6.8 Hz, 3 H, CH$_3$), 4.49 (d, J = 5.7 Hz, 2 H, NCH$_2$), 5.36 (q, J = 6.8 Hz, 1 H, OCHCO), 5.91 (dd, J = 10.4, 1.1 Hz, 1 H, CH$_2$CHCO), 6.15 (dd, J = 17.3, 10.2 Hz, 1 H, CH$_2$CHCO), 6.29-6.52 (m, 1H, NH), 6.47 (dd, J = 17.3, 0.9 Hz, 1 H, CH$_2$CHCO), 7.14-7.46 (m, 5 H, 5 Ar-H); $^{13}$C NMR (CDCl$_3$, 75 MHz): $\delta$ (ppm) = 17.75, 42.86, 70.50, 127.29, 127.32, 127.53, 128.50, 131.99, 137.86, 164.70, 170.34; FAB of C$_{13}$H$_{15}$NO$_3$ (M+H$^+$ = 234.0); HRMS (FAB) of C$_{13}$H$_{15}$NO$_3$ [M+H]$^+$ calc. 234.1128, found 234.1130; IR (ATR) $\nu$ = 3263.3, 3101.3, 3032.8, 2981.6, 2918.7, 1718.7, 1658.9, 1617.9, 1569.2, 1495.6, 1453.7, 1434.4, 1407.3, 1355.5, 1324.3, 1272.3, 1253.5, 1191.0, 1142.6, 1096.5, 1080.7, 1065.3, 1051.3, 1031.0, 1000.8, 965.8, 885.0, 853.5, 815.0, 736.6, 698.7, 672.9, 591.2, 513.8, 474.3, 449.5 cm$^{-1}$; $T_m$ = 67 °C (n-hexane/ethyl acetate).
1H-NMR (CDCl₃, 300 MHz)

13C-NMR (CDCl₃, 75 MHz)
1.2.9 Methyl 4-(2-(acryloyloxy)propanamido)butanoate (4i)

The Passerini 3-CR of acrylic acid 1 (721 mg, 6.86 µL, 10.0 mmol), acetaldehyde 3e (441 mg, 10.0 mmol) and methyl 4-isocyanobutyrate 2e (1.27 g, 10.0 mmol) in dichloromethane led to the formation of methyl 4-(2-(acryloyloxy)propanamido)butanoate. After purification by column chromatography (n-hexane/ethyl acetate 2:1), 4i was obtained as a brown liquid (2.27 g, 94%). TLC R<sub>f</sub> = 0.17 (n-hexane/ethyl acetate = 2:1); <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ (ppm) = 1.43 (d, J = 6.9 Hz, 3 H, CH<sub>3</sub>), 1.70-1.86 (m, 2 H, CH<sub>2</sub>), 2.31 (t, J = 7.1 Hz, 2 H, COCH<sub>2</sub>), 3.16-3.31 (m, 2 H, NCH<sub>2</sub>), 3.60 (s, 3H, COOCH<sub>3</sub>), 5.19 (q, J = 6.8 Hz, 1 H, OCHCO), 6.14 (dd, J = 17.3, 10.4 Hz, 1 H, CH<sub>2</sub>CHCO), 6.44 (dd, J = 17.3, 1.3 Hz, 1 H, CH<sub>2</sub>CHCO), 6.49-6.74 (m, 1H, NH); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz): δ (ppm) = 17.90, 24.26, 31.44, 38.79, 51.73, 70.59, 127.74, 132.15, 164.73, 170.51, 173.96; FAB of C<sub>11</sub>H<sub>17</sub>NO<sub>5</sub> (M+H<sup>+</sup> = 244.1); HRMS (FAB) of C<sub>11</sub>H<sub>17</sub>NO<sub>5</sub> [M+H]<sup>+</sup> calc. 244.1185, found 244.1183; IR (KBr) ν = 3314.3, 3093.7, 2952.6, 1730.8, 1665.6, 1543.3, 1440.0, 1408.2, 1371.5, 1294.2, 1261.7, 1190.3, 1097.3, 986.1, 875.9, 810.6, 676.1 cm<sup>-1</sup>.

24
1.3 Free radical polymerization

![Reaction scheme]

<table>
<thead>
<tr>
<th>polymer</th>
<th>monomer</th>
<th>$M_n$ [g/mol]</th>
<th>PDI</th>
<th>Yield [%]</th>
<th>$T_g$ [°C]</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1</td>
<td>4a</td>
<td>43100</td>
<td>2.11</td>
<td>75</td>
<td>123</td>
</tr>
<tr>
<td>P2</td>
<td>4b</td>
<td>59550</td>
<td>2.11</td>
<td>79</td>
<td>59</td>
</tr>
<tr>
<td>P3</td>
<td>4c</td>
<td>98500</td>
<td>2.51</td>
<td>74</td>
<td>111</td>
</tr>
<tr>
<td>P4</td>
<td>4d</td>
<td>56100</td>
<td>2.60</td>
<td>65</td>
<td>96</td>
</tr>
<tr>
<td>P5</td>
<td>4e</td>
<td>88250</td>
<td>2.25</td>
<td>67</td>
<td>104</td>
</tr>
<tr>
<td>P6</td>
<td>4f</td>
<td>45500</td>
<td>3.40</td>
<td>86</td>
<td>122</td>
</tr>
<tr>
<td>P7</td>
<td>4g</td>
<td>29150</td>
<td>4.16</td>
<td>81</td>
<td>51</td>
</tr>
<tr>
<td>P8</td>
<td>4h</td>
<td>26100</td>
<td>3.31</td>
<td>75</td>
<td>85</td>
</tr>
<tr>
<td>P9</td>
<td>4i</td>
<td>45500</td>
<td>5.96</td>
<td>84</td>
<td>30</td>
</tr>
</tbody>
</table>

**General procedure:**

2.00 mmol of the corresponding acrylate monomer and 1.0 mol% of AIBN (3.3 mg, 0.02 mmol) are dissolved in ethyl acetate (2.20 mL). Then, the reaction mixture is degassed with argon for 10 min and afterwards the polymerization was performed at 70 °C for 6 h. After this period of time, the solution is slowly dropped into cold diethyl ether. The precipitated polymers are separated by filtration and dried in vacuum to obtain polyacrylates.
1.3.1 Polyacrylate derived from monomer 4a (P1)

![Polyacrylate structure](image)

The free radical polymerization of monomer 4a (523 mg, 2.00 mmol) yielded polyacrylate P1 as colorless solid (392 mg, 75 %). $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ (ppm) = 1.22 (s, 9 H, 3 CH$_3$), 1.41-2.19 (m, 2 H, CH$_2$ backbone), 2.19-3.03 (m, 1 H, CH backbone), 5.47-6.00 (m, 1 H, OCHCO), 6.00-6.76 (br, 1 H, NH), 7.00-7.79 (m, 5 H, Ar-H); $T_g$ = 123°C.

$^1$H-NMR (CDCl$_3$, 300 MHz)
1.3.2 Polyacrylate derived from monomer 4b (P2)

The free radical polymerization of monomer 4b (539 mg, 2.00 mmol) yielded polyacrylate P2 as colorless solid (423 mg, 79%). $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ (ppm) = 0.72-1.00 (m, 3 H, CH$_3$), 1.00-2.15 (m, 12 H, 5 CH$_2$ and CH$_2$ backbone), 1.33 (s, 9 H, 3 CH$_3$), 2.15-2.87 (m, 1 H, CH backbone), 4.47-5.18 (m, 1 H, OCHCO), 5.90-6.92 (br, 1 H, NH); $T_g$ = 59°C.

$^1$H-NMR (CDCl$_3$, 300 MHz)
1.3.3 Polyacrylate derived from monomer 4c (P3)

The free radical polymerization of monomer 4c (455 mg, 2.00 mmol) yielded polyacrylate P3 as colorless solid (337 mg, 74 %). \(^1\)H NMR (CDCl\(_3\), 300 MHz): \(\delta\) (ppm) = 0.72-1.10 (m, 6 H, 2 CH\(_3\)), 1.32 (s, 9 H, 3 CH\(_3\)), 1.51-2.89 (m, 4 H, CH(CH\(_3\))\(_2\), CH\(_2\) and CH backbone), 4.27-5.09 (m, 1 H, OCHCO), 5.68-6.82 (br, 1 H, NH); \(T_g = 111^\circ\)C.
1.3.4 Polyacrylate derived from monomer 4d (P4)

The free radical polymerization of monomer 4d (427 mg, 2.00 mmol) yielded polyacrylate P4 as colorless solid (278 mg, 65 %). $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ (ppm) = 0.78-1.01 (m, 3 H, CH$_3$), 1.33 (s, 9 H, 3 CH$_3$), 1.48-2.12 (m, 4 H, CH$_2$, CH$_2$ backbone), 2.21-2.88 (m, 1 H, CH backbone), 4.57-5.10 (m, 1 H, OCHCO), 5.97-6.89 (br, 1 H, NH); $T_g = 96^\circ$C.

$^1$H-NMR (CDCl$_3$, 300 MHz)
1.3.5 Polyacrylate derived from monomer 4e (P5)

The free radical polymerization of monomer 4e (399 mg, 2.00 mmol) yielded polyacrylate P5 as colorless solid (266 mg, 67 %). $^1$H NMR (CDCl3, 300 MHz): $\delta$ (ppm) = 1.33 (s, 9 H, 3 CH3), 1.35-1.45 (m, 3 H, CH3), 1.58-2.15 (m, 2 H, CH2 backbone), 2.20-2.69 (m, 1 H, CH backbone), 4.69-5.08 (m, 1 H, OCHCO), 6.03-6.70 (br, 1 H, NH); $T_g$ = 104°C.

$^1$H-NMR (CDCl3, 300 MHz)
1.3.6 Polyacrylate derived from monomer 4f (P6)

The free radical polymerization of monomer 4f (451 mg, 2.00 mmol) yielded polyacrylate P6 as colorless solid (387 mg, 86 %). $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ (ppm) = 0.85-2.21 (m, 12 H, 5 CH$_2$ and CH$_2$ backbone), 1.42 (m, 3 H, CH$_3$), 2.21-2.82 (m, 1 H, CH backbone), 3.53-3.96 (m, 1 H, NCH), 4.73-5.23 (m, 1 H, OCHCO), 6.36-7.27 (m, 1H, NH); $T_g = 122^\circ$C.

$^1$H-NMR (CDCl$_3$, 300 MHz)
1.3.7 Polyacrylate derived from monomer 4g (P7)

The free radical polymerization of monomer 4g (427 mg, 2.00 mmol) yielded polyacrylate P7 as colorless solid (345 mg, 81%). $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ (ppm) = 0.87 (t, J = 5.9 Hz, 3 H, CH$_3$), 1.03-2.19 (m, 11 H, 3 CH$_2$, CH$_3$ and CH$_2$ backbone), 2.20-2.79 (m, 1 H, CH backbone), 2.87-3.49 (m, 2 H, NCH$_2$), 4.76-5.35 (m, 1 H, OCHCO), 6.60-7.55 (m, 1H, NH); $T_g = 51^\circ$C.

$^1$H-NMR (CDCl$_3$, 300 MHz)
1.3.8 Polyacrylate derived from monomer 4h (P8)

The free radical polymerization of monomer 4h (467 mg, 2.00 mmol) yielded polyacrylate P8 as colorless solid (352 mg, 75 %). $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ (ppm) = 0.79-1.59 (m, 3 H, CH$_3$), 1.29-2.16 (m, 2 H, CH$_2$ backbone), 2.16-2.80 (m, 1 H, CH backbone), 3.86-4.49 (m, 2 H, NCH$_2$), 4.64-5.21 (m, 1 H, OCHCO), 6.73-7.80 (m, 6 H, NH and 5 Ar-H); $T_g = 85^\circ$C.

$^1$H-NMR (CDCl$_3$, 300 MHz)

![NMR spectrum](image-url)
1.3.9 Polyacrylate derived from monomer 4i (P9)

The free radical polymerization of monomer 4i (487 mg, 2.00 mmol) yielded polyacrylate P9 as colorless solid (408 mg, 84 %). $^1$H NMR (CDCl$_3$, 300 MHz): $\delta$ (ppm) = 1.27-1.56 (m, 3 H, CH$_3$), 1.58-2.18 (m, 4 H, CH$_2$ and CH$_2$ backbone), 2.24-2.44 (m, 2 H, CH$_2$COO), 2.24-2.65 (m, 1 H, CH backbone), 3.06-3.41 (m, 2 H, NCH$_2$), 3.65 (s, 3 H, CH$_3$), 4.81-5.23 (m, 1 H, OCHCO), 6.94-7.66 (m, 1 H, NH); $T_g = 30^\circ$C.

$^1$H-NMR (CDCl$_3$, 300 MHz)
2. UCST measurements

For the experiments, the complete solubility range of the corresponding solvent was examined by cooling down to -78°C and slowly heating up until the boiling point of the solvent. For indication of the LCST/UCST behavior, we determined the temperature when the solution was completely clear or turbid.

2.1 UCST (6-28°C) of P6 in methanol
2.2 UCST (55-74°C) of P8 in ethanol
2.3 UCST (6-19°C) of P9 in ethanol
2.4 UCST (-37 - -20°C) of P9 in methanol
3. References
