Tunable polymers obtained from Passerini multicomponent reaction derived acrylate monomers

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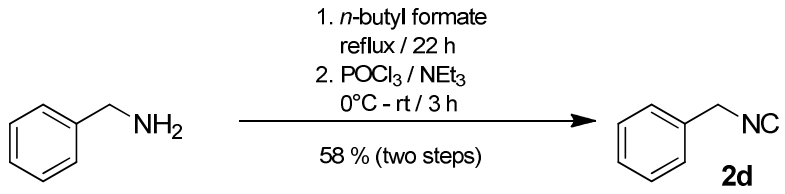
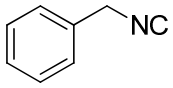
1. Supporting Information

1.1 Isocyanide syntheses[iii]



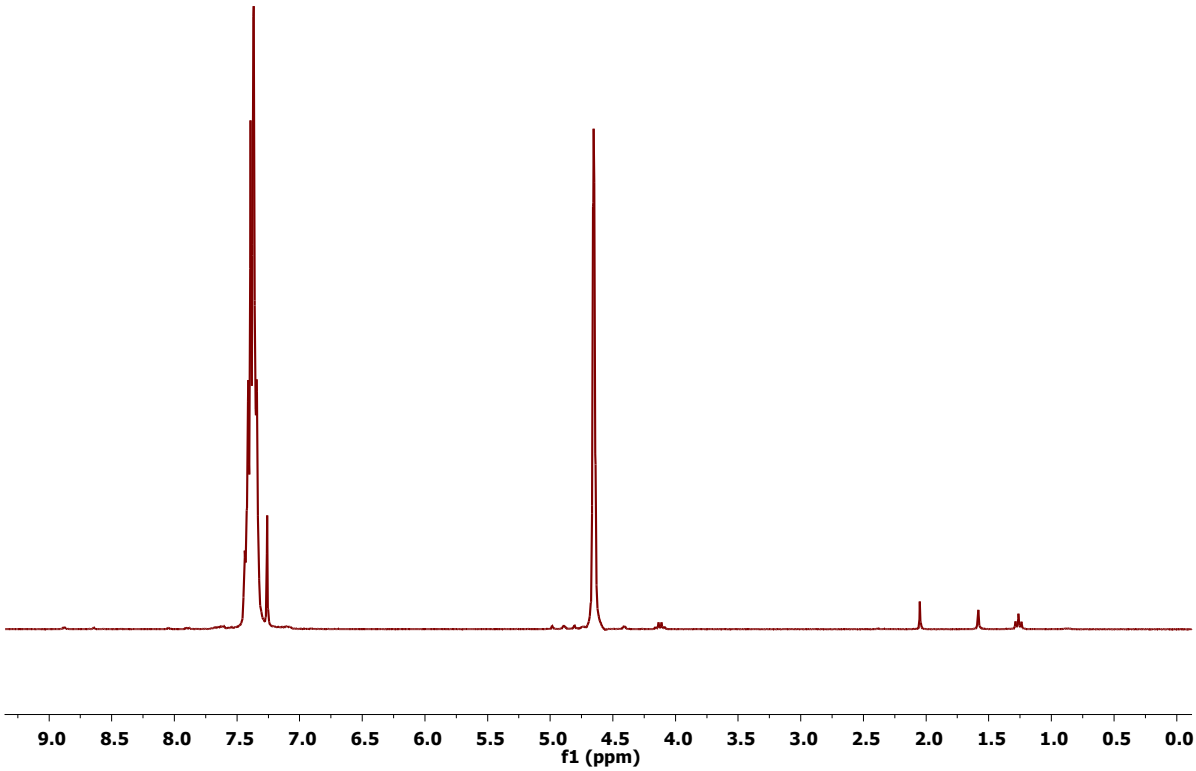
1.1.1 Benzyl isocyanide (2d)



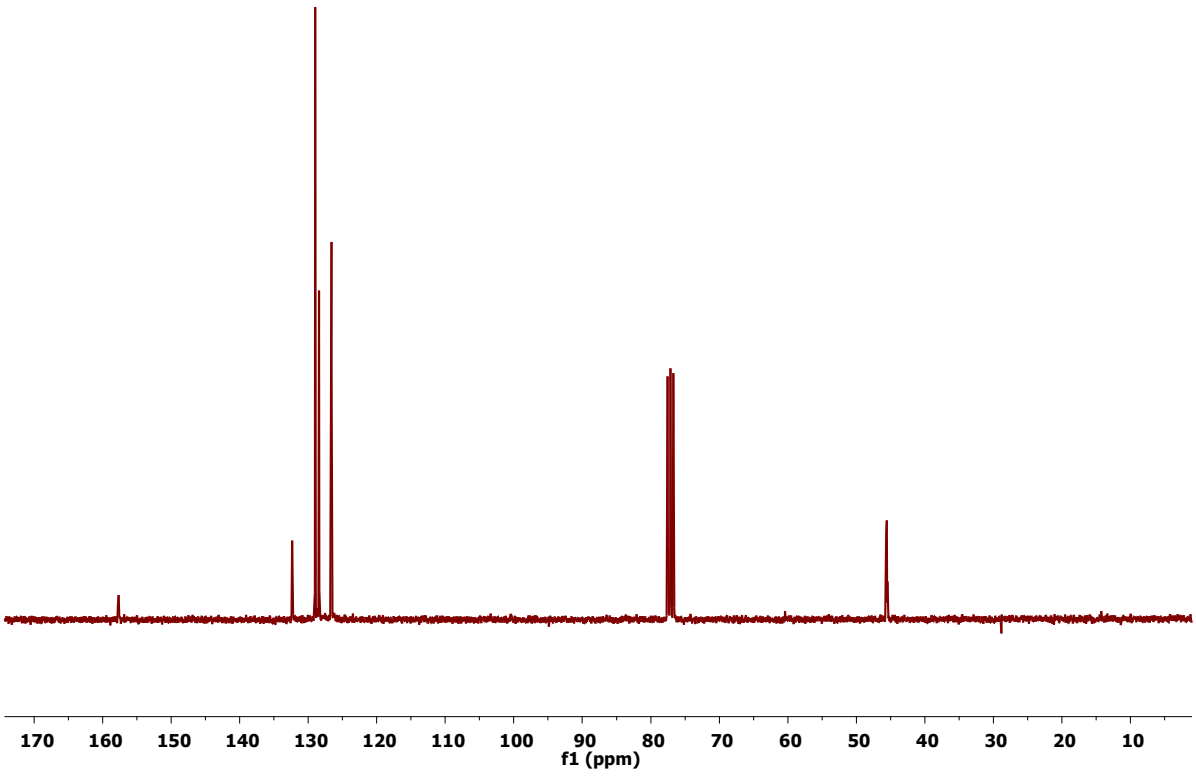
A mixture of benzylamine (5.00 g, 5.09 mL, 46.7 mmol), *n*-butylformate (53.6 g, 55.9 mL, 525 mmol) and triethylamine (9 mL) was dissolved in 90 mL xylene and refluxed for 22 hours. Then, the reaction mixture was evaporated under reduced pressure and the residue was recrystallized from hexane to yield *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): δ (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).

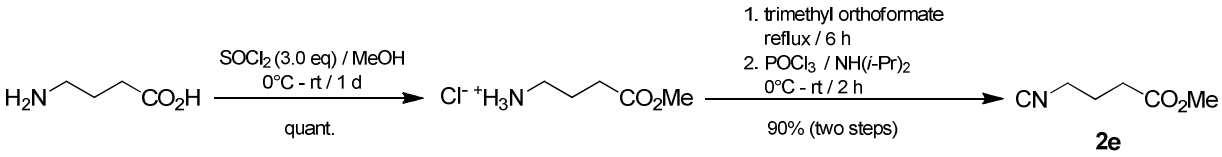
N-benzylformamide (5.75 g, 42.6 mmol) was dissolved in 40 mL dichloromethane and 4.3 mL triethylamine (31 mmol) were added. The mixture was cooled down with a NaCl ice bath. Subsequently, $POCl_3$ (7.18 g, 4.27 mL, 46.8 mmol) was slowly added. Then, the reaction mixture was allowed to warm up at room 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_2SO_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): δ (ppm) = 4.65 (s, 2 H, CH_2), 7.30-7.50 (m, 5 H, Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 45.48, 45.58, 45.68, 126.67, 128.47, 129.04, 132.40, 157.66, 157.73, 157.80.

1H-NMR (CDCl3, 300 MHz)

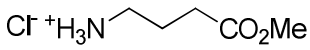


13C-NMR (CDCl3, 75 MHz)

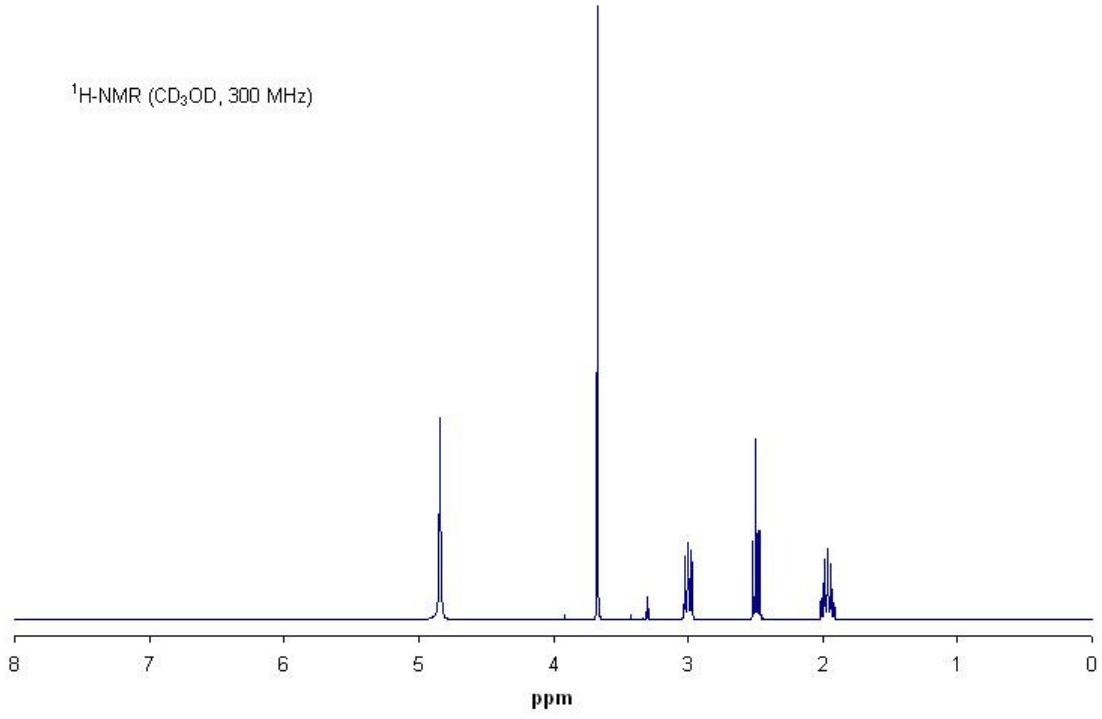


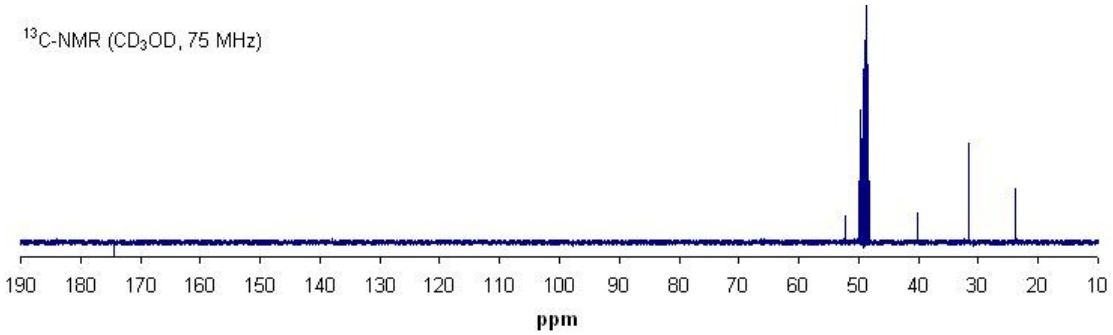


1.1.2 Methyl 4-aminobutyrate hydrochloride

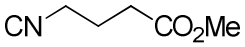


4-Aminobutyric acid (GABA, 20.0 g, 194 mmol) was suspended in methanol (300 mL) and cooled down with an ice bath to 0°C. Subsequently, thionyl chloride (71.4 g, 600 mmol, 3.0 eq.) was dropped to the strongly stirred solution. Then, the reaction mixture was allowed to reach room temperature and was stirred 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_3OD, 300 MHz) δ (ppm) = 1.96 (quint., J = 7.4 Hz, 2 H, CH_2), 2.50 (t, J = 7.2 Hz, 2 H, C**H$_2$**CO_2Me), 3.00 (t, J = 7.6 Hz, 2 H, C**H$_2$**NH_3^+), 3.69 (s, 3 H, COOC**H$_3$**); ^{13}C NMR (CD_3OD, 75 MHz) δ (ppm) = 23.7 (**C**H_2), 31.4 (**C**H_2CO_2Me), 40.0 (**C**$H_2NH_3^+$), 52.3 (COO**C**H_3), 174.5 (**C**O_2Me); FAB of $C_5H_{12}NO_2$ (M^+ = 118.3). T_m = 120-121°C (diethyl ether).





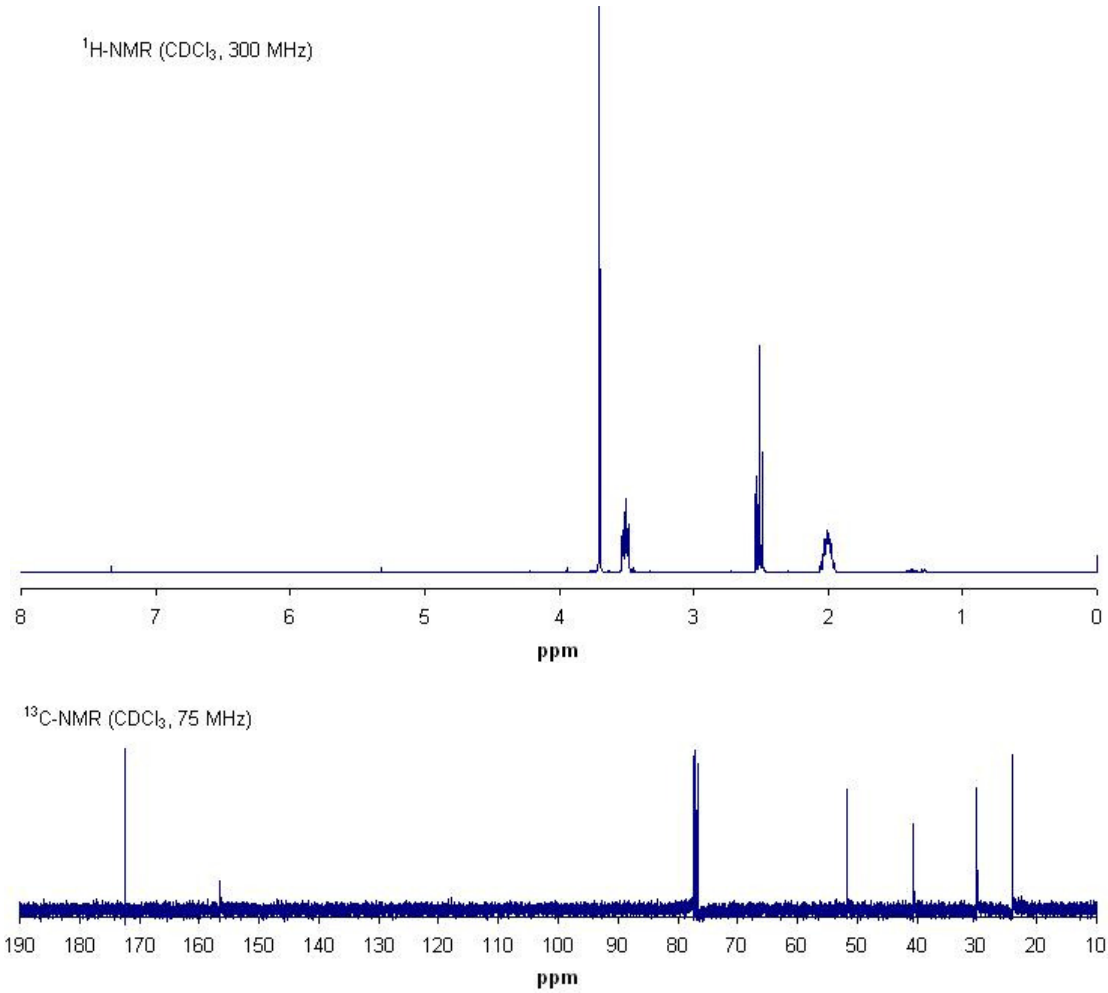
1.1.3 Methyl 4-isocyanobutyrate (2e)



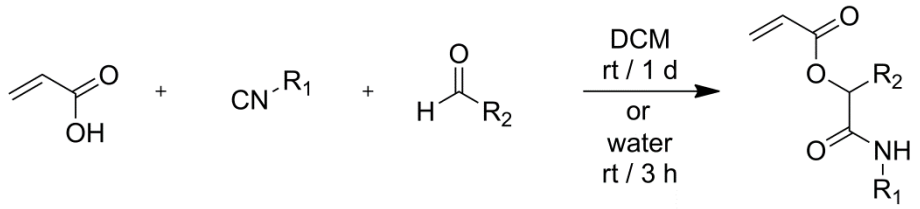
Methyl 4-aminobutyrate hydrochloride (20.0 g, 130 mmol) was suspended in trimethyl orthoformate (45 mL) and heated to reflux under stirring. The reaction progress was controlled by TLC (dichloromethane/ methanol 9:1) and after six hours a full conversion was detected. Then the reaction mixture was evaporated 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) δ (ppm) = 1.87 (quint., J = 7.2 Hz, 2 H, C**H$_2$**), 2.40 (t, J = 7.2 Hz, 2 H, C**H$_2$**CO_2Me), 3.34 (q, J = 6.8 Hz, 2 H, C**H$_2$**NH), 3.68 (s, 3 H, COOC**H$_3$**), 6.67 (br, s, 1 H, N**H**), 8.03 (d, J = 11.7 Hz, 1 H, NHC**H**O, *cis*), 8.16 (s, 1 H, NHC**H**O, *trans*); FAB of $C_6H_{11}NO_3$ ($M+H^+$ = 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) δ (ppm) = 1.97-2.04 (m, 2 H, C**H$_2$**), 2.52 (t, J = 7.0 Hz, 2 H,

C**H₂**CO_2Me), 3.49-3.53 (m, 2 H, C**H₂**NC), 3.71 (s, 3 H, COOC**H₃**); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) = 24.1 (**C**H_2), 30.0 (**C**H_2CO_2Me), 40.7 (triplet, **C**H_2NC), 51.7 (COO**C**H_3), 156.5 (triplet, –N**C**) 172.4 (**C**O_2Me); IR (ATR) ν = 2148.5 (NC), 1731.5 (CO_2Me) cm^{-1}.



1.2 Monomer syntheses



1 **2a-2e** **3a-3e** **4a-4i**

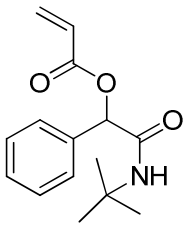
product	R^1	R^2	solvent	yield [%]
4a	-*t*-Bu (**2a**)	-Ph (**3a**)	water / DCM	41 / 12
4b	-*t*-Bu (**2a**)	-$(CH_2)_5CH_3$ (**3b**)	water / DCM	68 / 45
4c	-*t*-Bu (**2a**)	-*i*-Pr (**3c**)	water / DCM	74 / 89
4d	-*t*-Bu (**2a**)	-Et (**3d**)	water / DCM	67 / 77
4e	-*t*-Bu (**2a**)	-Me (**3e**)	DCM	86
4f	-*c*-Hx (**2b**)	-Me (**3e**)	DCM	100
4g	-$(CH_2)_4CH_3$ (**2c**)	-Me (**3e**)	DCM	100
4h	-Bn (**2d**)	-Me (**3e**)	DCM	74
4i	-$(CH_2)_3CO_2Me$ (**2e**)	-Me (**3e**)	DCM	94

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).

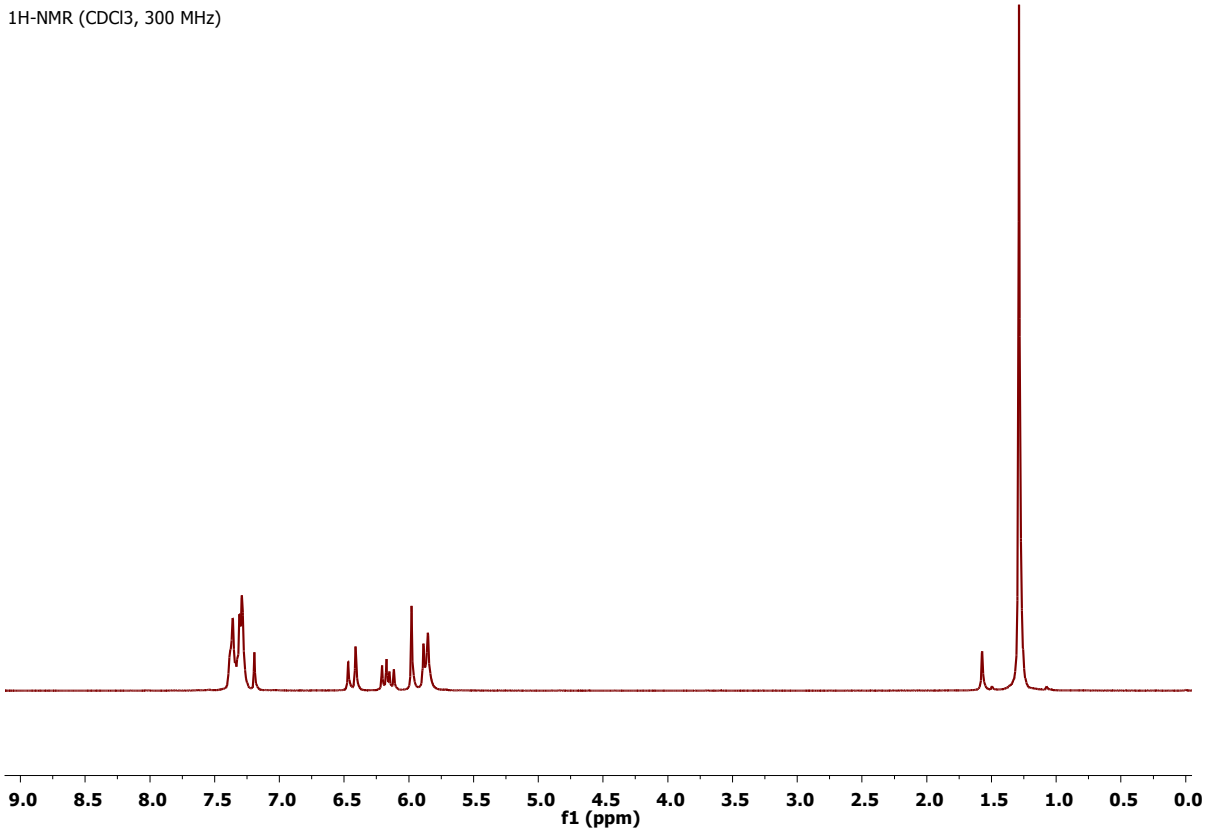
Alternative procedure in deionized water: Freshly distilled acrylic acid **1** (721 mg, 686 µL, 10.0 mmol), the desired aldehyde **3a-d** (10.0 mmol) and 20 mL water were mixed together in a round bottom flask. Subsequently, *tert*-butyl isocyanide **2a** (831 mg, 1.13 mL, 10.0 mmol) was added under 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**)

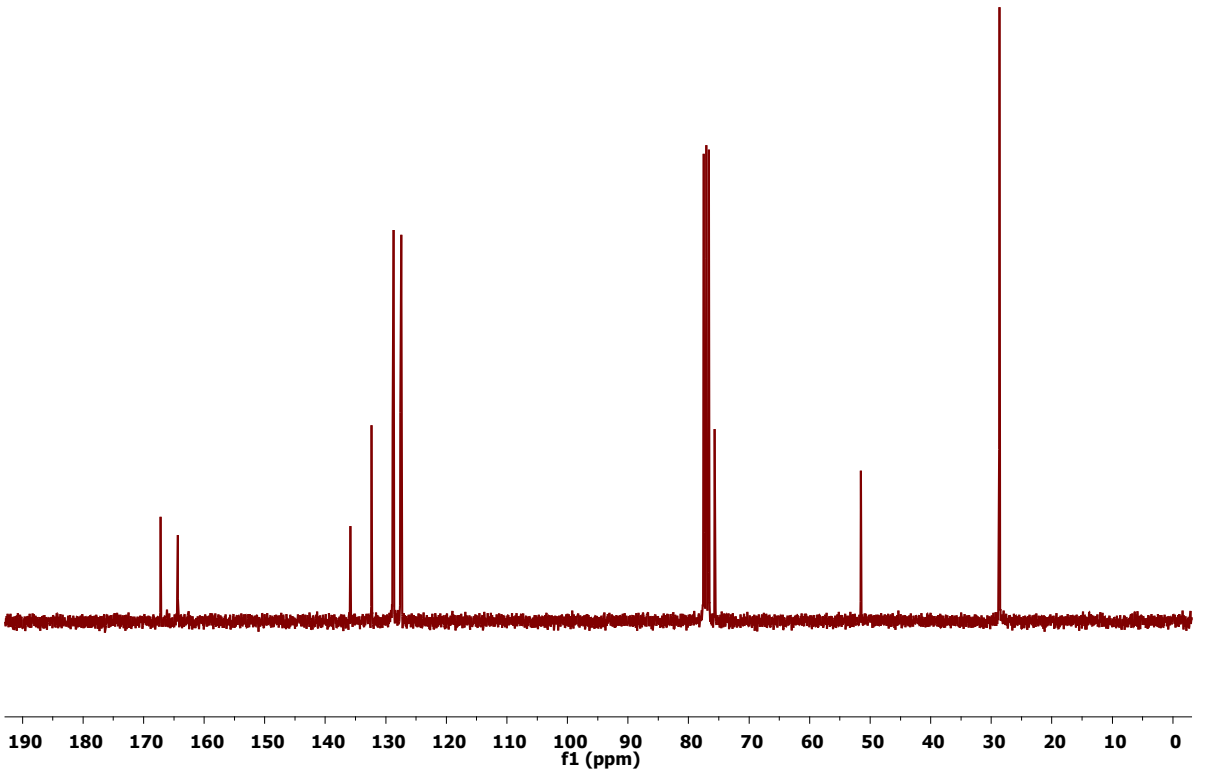


The Passerini-3CR of acrylic acid **1** (721 mg, 686 µL, 10.0 mmol), benzaldehyde **3a** (1.06 g, 1.01 mL, 10.0 mmol) and *tert*-butyl isocyanide **2a** (831 mg, 1.13 mL, 10.0 mmol) in water led to the formation of 2-(*tert*-butylamino)-2-oxo-1-phenylethyl acrylate. Direct Filtration yielded **4a** as 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): δ (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, C**H**$_2$CHCO), 6.05 (s, 1H, OCH), 6.23 (dd, J = 17.3, 10.4 Hz, 1 H, CH_2C**H**CO), 6.51 (dd, J = 17.3, 1.1 Hz, 1 H, C**H**$_2$CHCO), 7.30-7.52 (m, 5 H, 5 Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 28.75, 51.65, 75.78, 127.54, 127.71, 128.83, 128.99, 132.48, 135.93, 164.46, 167.32; FAB of $C_{15}H_{19}NO_3$ (M^+ = 261.9); HRMS (FAB) of $C_{15}H_{19}NO_3$ $[M+H]^+$ calc. 262.1443, found 262.1441; IR (ATR) ν = 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).

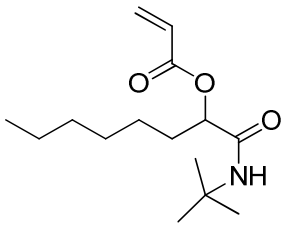
1H-NMR (CDCl3, 300 MHz)



13C-NMR (CDCl3, 75 MHz)

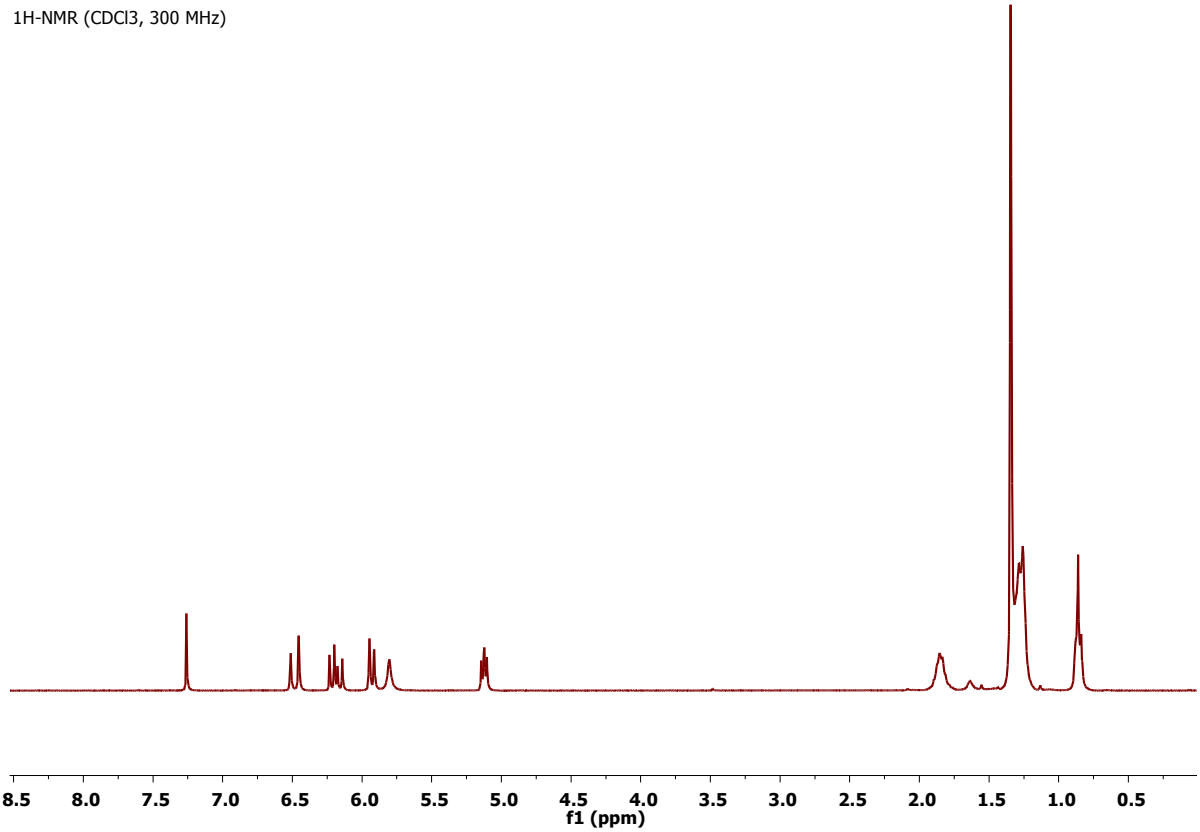


1.2.2 1-(*tert*-Butylamino)-1-oxooctan-2-yl acrylate (**4b**)

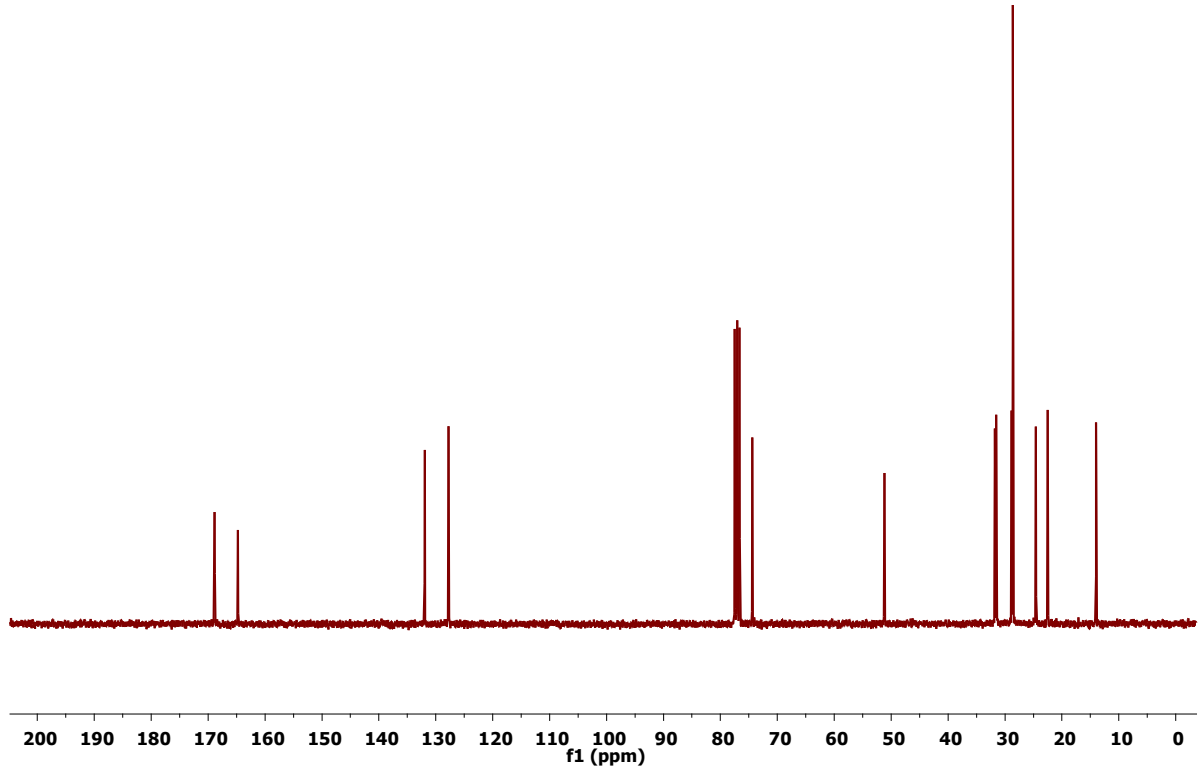


The Passerini-3CR of acrylic acid **1** (721 mg, 686 µL, 10.0 mmol), heptanal **3b** (1.14 g, 1.41 mL, 10.0 mmol) and *tert*-butyl isocyanide **2a** (831 mg, 1.13 mL, 10.0 mmol) in water led to the formation of 1-(*tert*-butylamino)-1-oxooctan-2-yl acrylate. Direct Filtration yielded **4b** as a colorless solid (1.82 g, 68 %). TLC R_f = 0.42 (*n*-hexane/ethyl acetate = 4:1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ (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, CHC**H**$_2$), 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, C**H**$_2$CHCO), 6.19 (dd, J = 17.3, 10.4 Hz, 1 H, CH_2C**H**CO), 6.48 (dd, J = 17.3, 1.1 Hz, 1 H, C**H**$_2$CHCO); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (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) ν = 3307.3, 2957.0, 2926.4, 2858.6, 1728.0, 1659.1, 1619.2, 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 °C (water).

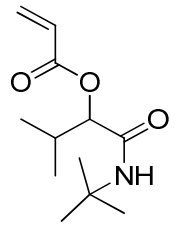
1H-NMR (CDCl3, 300 MHz)



13C-NMR (CDCl3, 75 MHz)

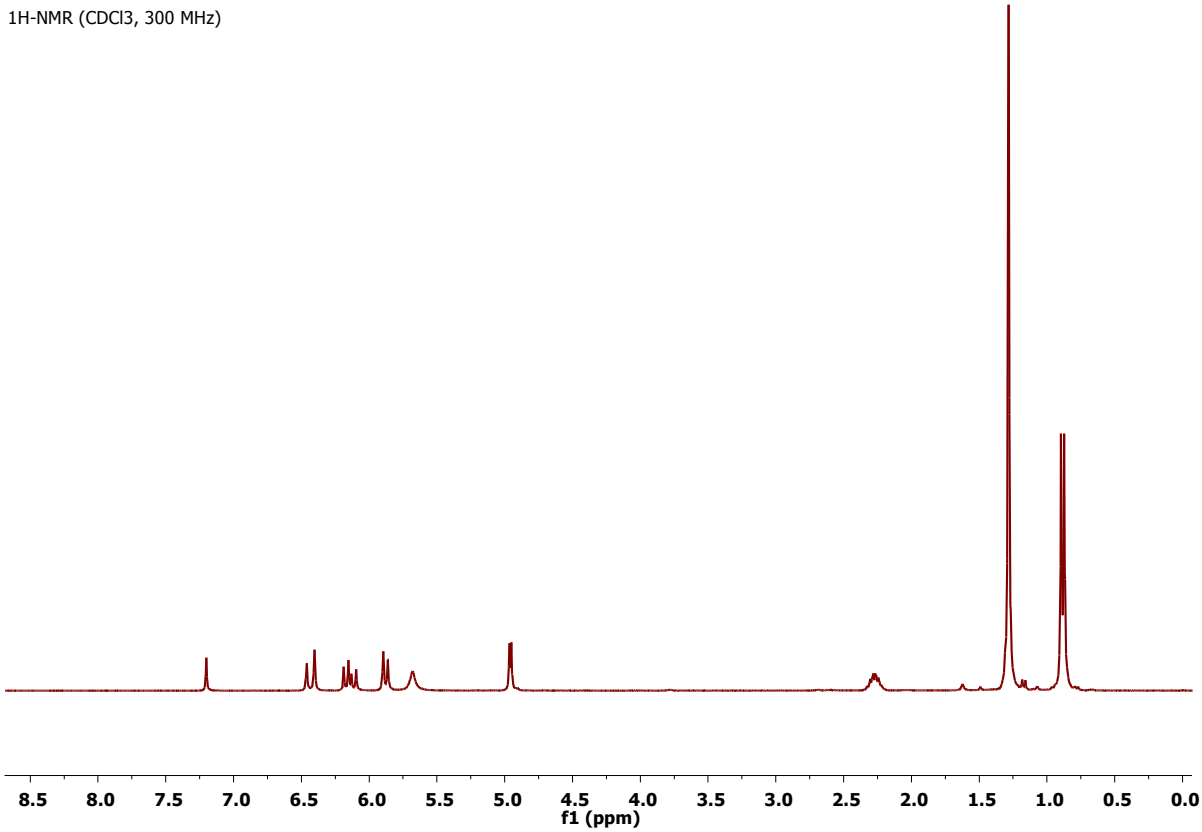


1.2.3 1-(*tert*-Butylamino)-3-methyl-1-oxobutan-2-yl acrylate (4c)

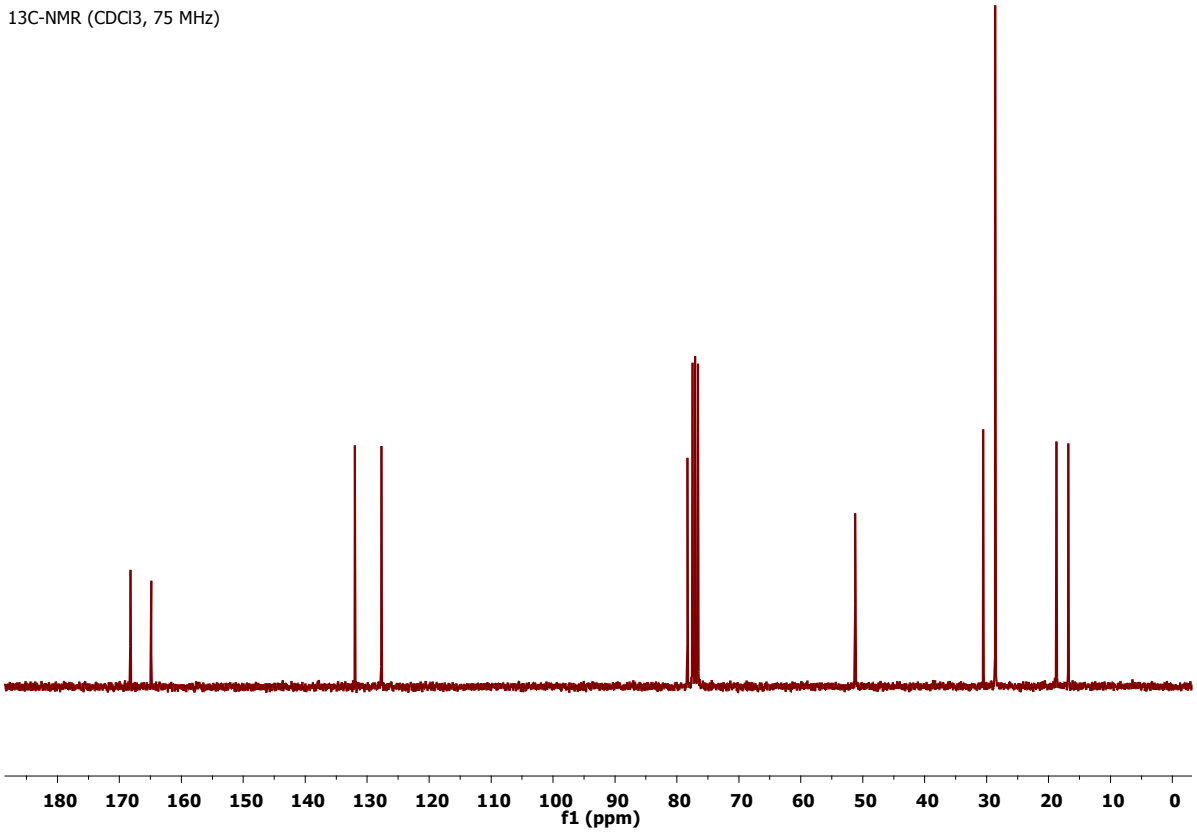


The Passerini-3CR of acrylic acid **1** (721 mg, 686 µL, 10.0 mmol), isobutyraldehyde **3c** (721 mg, 913 µL, 10.0 mmol) and *tert*-butyl isocyanide **2a** (831 mg, 1.13 mL, 10.0 mmol) in water led to the formation of 1-(*tert*-butylamino)-3-methyl-1-oxobutan-2-yl acrylate. Direct Filtration yielded **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): δ (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, C**H**$_2$CHCO), 6.20 (dd, J = 17.3, 10.4 Hz, 1 H, CH_2C**H**CO), 6.49 (dd, J = 17.3, 1.2 Hz, 1 H, C**H**$_2$CHCO); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (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) ν = 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).

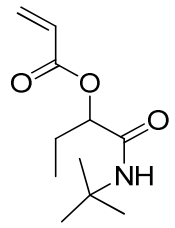
1H-NMR (CDCl3, 300 MHz)



13C-NMR (CDCl3, 75 MHz)

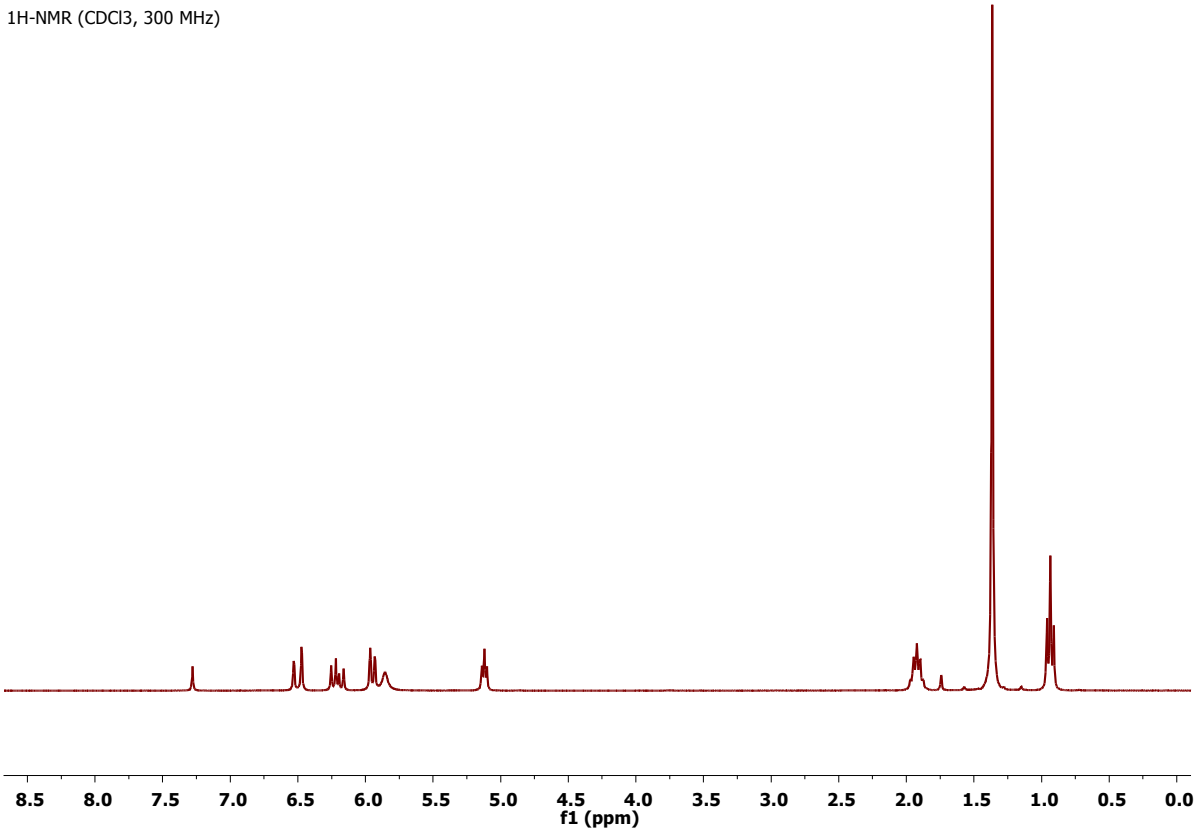


1.2.4 1-(*tert*-Butylamino)-1-oxobutan-2-yl acrylate (4d)

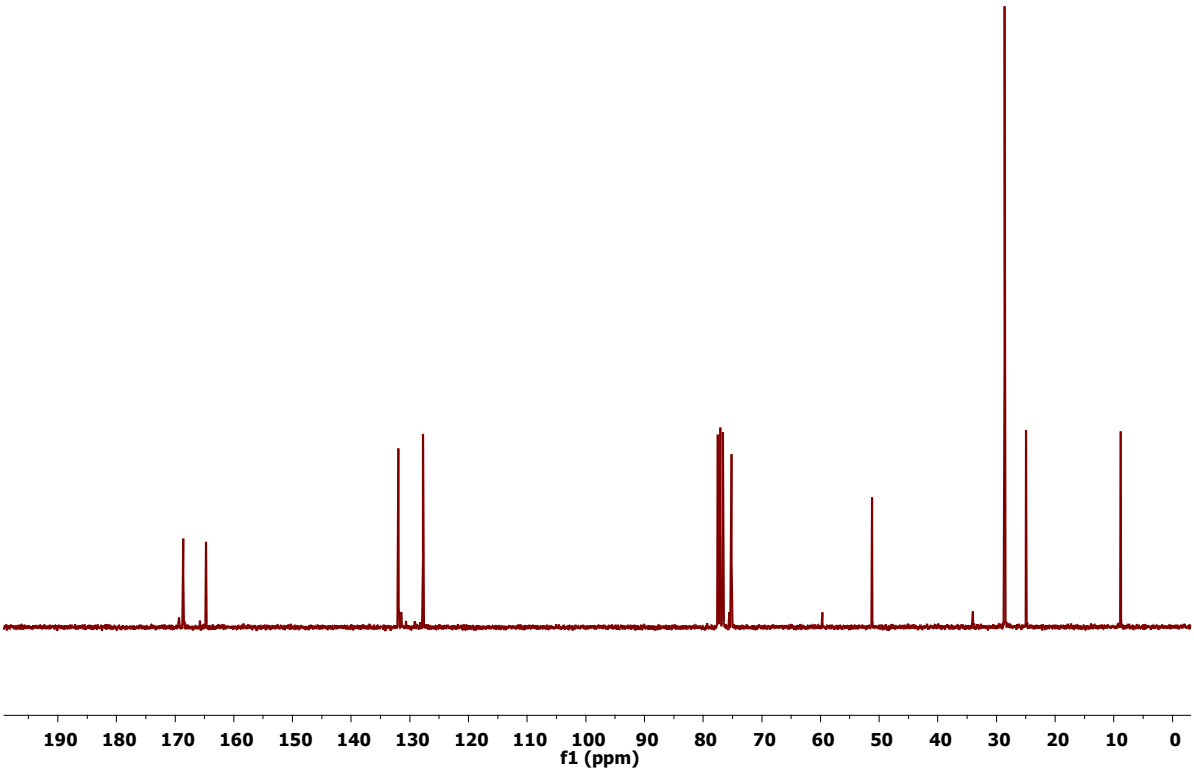


The Passerini-3CR of acrylic acid **1** (721 mg, 686 µL, 10.0 mmol), propionaldehyde **3d** (581 mg, 717 µL, 10.0 mmol) and *tert*-butyl isocyanide **2a** (831 mg, 1.13 mL, 10.0 mmol) in water led to the formation of 1-(*tert*-butylamino)-1-oxobutan-2-yl acrylate. Direct Filtration yielded **4d** as a colorless solid (1.43 g, 67 %). TLC (*n*-hexane/ethyl acetate = 4:1) R_f = 0.35; ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.92 (t, J = 7.5 Hz, 3 H, C**H**$_3$CH$_2$), 1.35 (s, 9 H, 3 CH$_3$), 1.83-1.97 (m, 2 H, CH$_2$), 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, C**H**$_2$CHCO), 6.19 (dd, J = 17.3, 10.4 Hz, 1 H, CH$_2$C**H**CO), 6.48 (dd, J = 17.3, 1.2 Hz, 1 H, C**H**$_2$CHCO); ^{13}C NMR ($CDCl_3$, 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 $C_{11}H_{19}NO_3$ (M^+ = 213.3); HRMS (FAB) of $C_{11}H_{19}NO_3$ $[M]^+$ 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}; T_m = 92 °C (water).

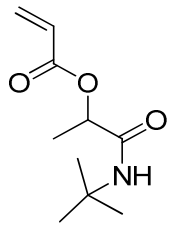
1H-NMR (CDCl3, 300 MHz)



13C-NMR (CDCl3, 75 MHz)

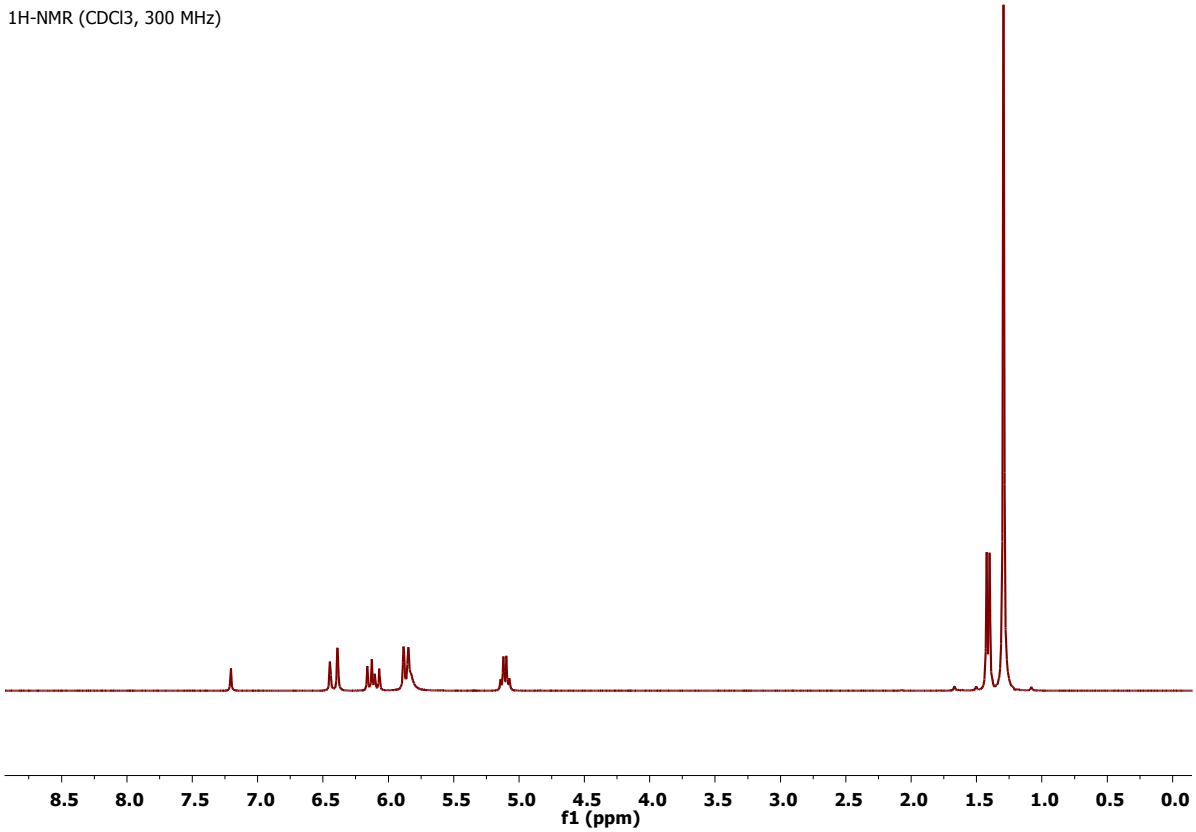


1.2.5 1-(*tert*-Butylamino)-1-oxopropan-2-yl acrylate (4e)

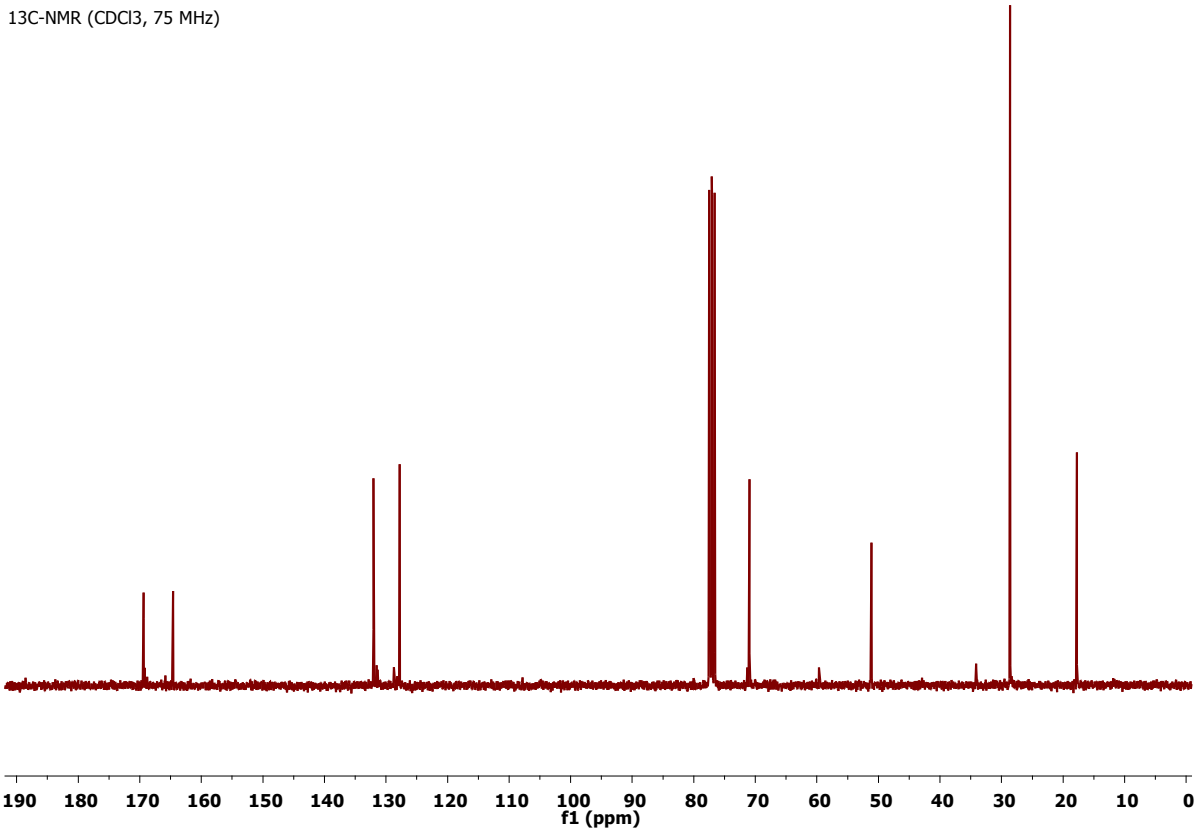


The Passerini 3-CR of acrylic acid **1** (721 mg, 686 µL, 10.0 mmol), acetaldehyde **3e** (441 mg, 10.0 mmol) and *tert*-butyl isocyanide **2a** (831 mg, 1.13 mL, 10.0 mmol) dichloromethane led to the formation of 1-(*tert*-butylamino)-1-oxopropan-2-yl acrylate. After purification by column chromatography (*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): δ (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, C**H**$_2$CHCO), 6.17 (dd, J = 17.3, 10.4 Hz, 1 H, CH_2C**H**CO), 6.48 (dd, J = 17.3, 1.0 Hz, 1 H, C**H**$_2$CHCO); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (ppm) = 17.88, 28.73, 51.26, 71.06, 127.90, 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) ν = 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).

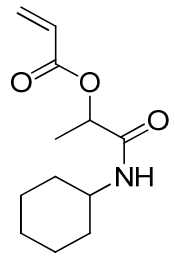
1H-NMR (CDCl3, 300 MHz)



13C-NMR (CDCl3, 75 MHz)

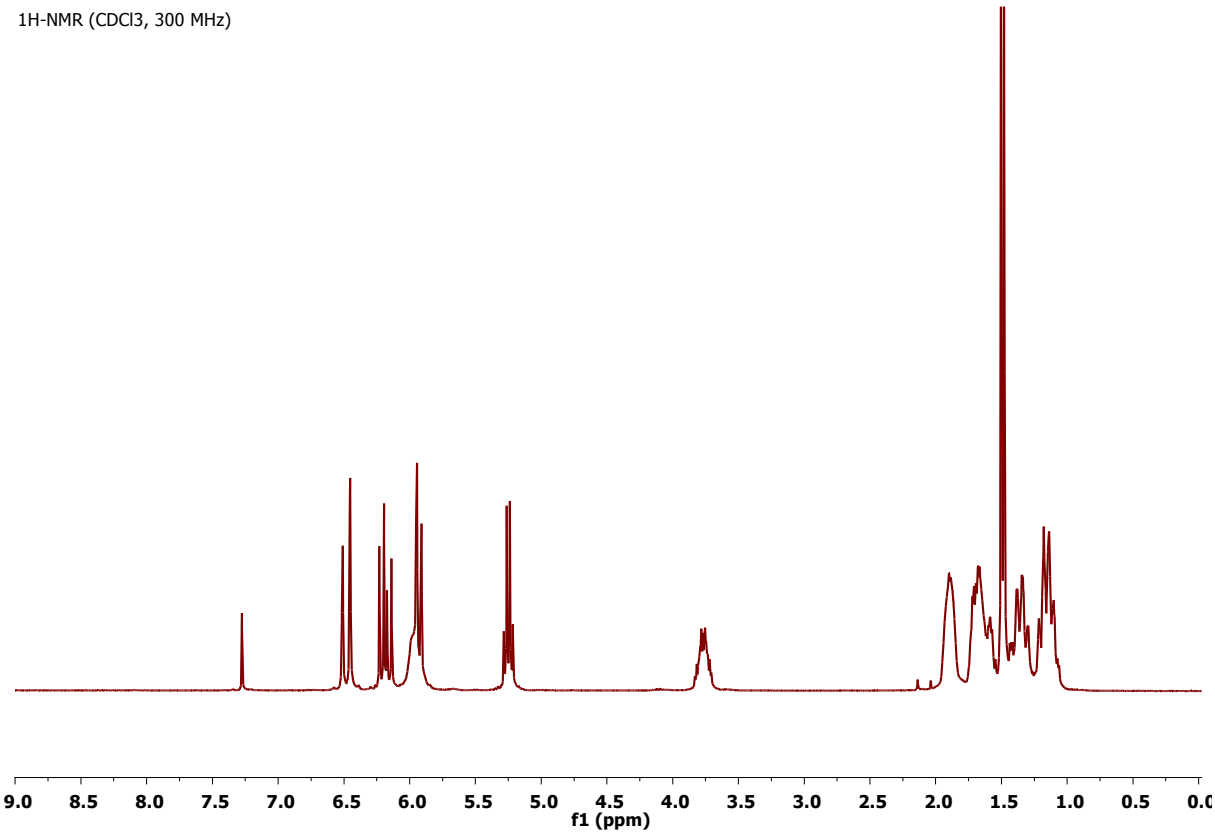


1.2.6 1-(Cyclohexylamino)-1-oxopropan-2-yl acrylate (**4f**)

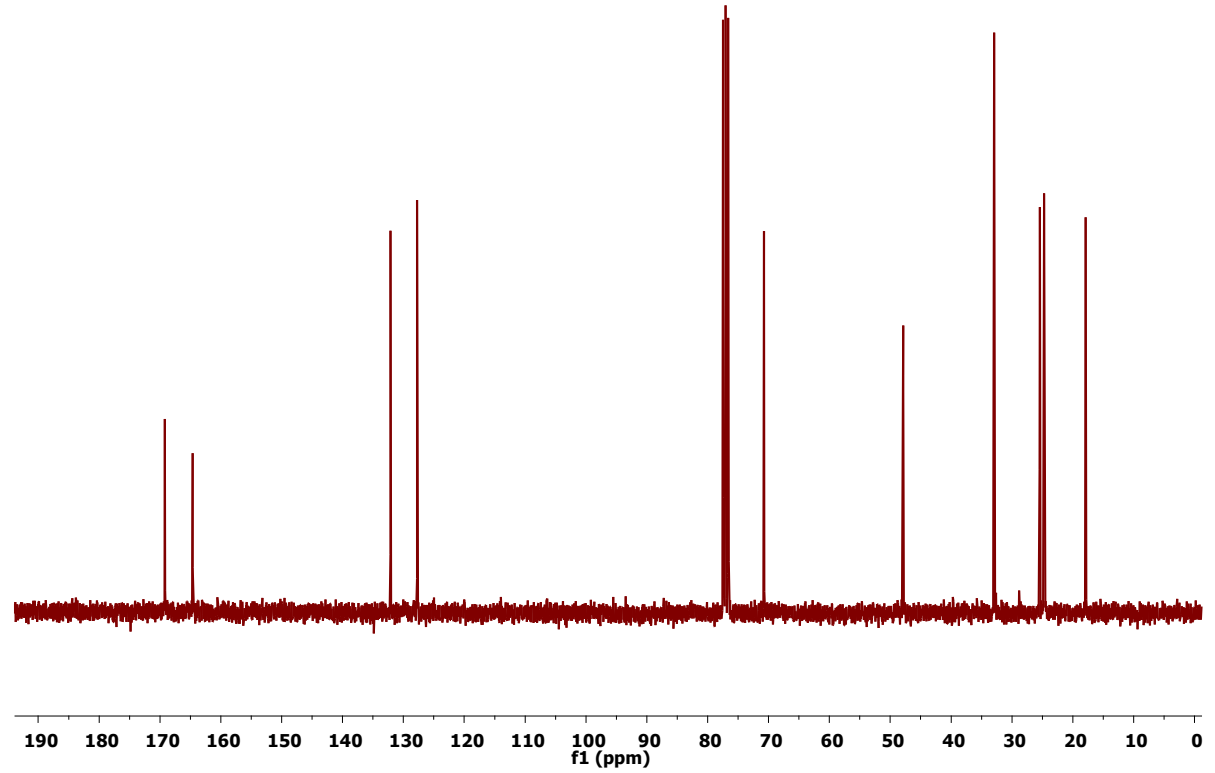


The Passerini 3-CR of acrylic acid **1** (721 mg, 686 µL, 10.0 mmol), acetaldehyde **3e** (441 mg, 10.0 mmol) and cyclohexyl isocyanide **2b** (1.09 g, 1.24 mL, 10.0 mmol) in dichloromethane led to the formation of 1-(cyclohexylamino)-1-oxopropan-2-yl acrylate. After drying in high vacuum, **4f** was 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): δ (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, C**H**$_2$CHCO), 6.17 (dd, J = 17.3, 10.4 Hz, 1 H, CH_2C**H**CO), 6.47 (dd, J = 17.3, 1.3 Hz, 1 H, C**H**$_2$CHCO); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (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) ν = 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°C (dichloromethane).

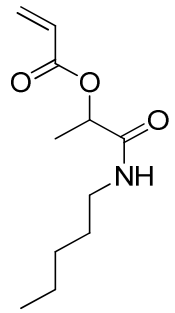
1H-NMR (CDCl3, 300 MHz)



13C-NMR (CDCl3, 75 MHz)

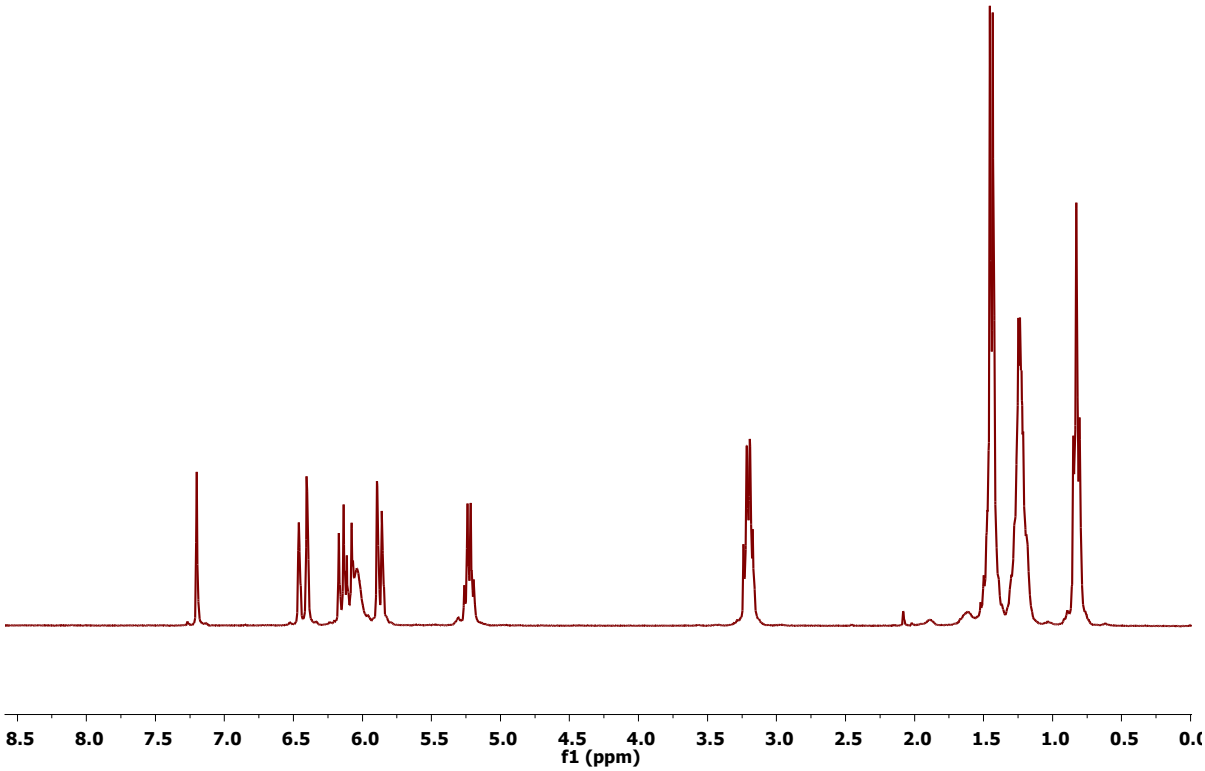


1.2.7 1-Oxo-1-(pentylamino)propan-2-yl acrylate (4g)

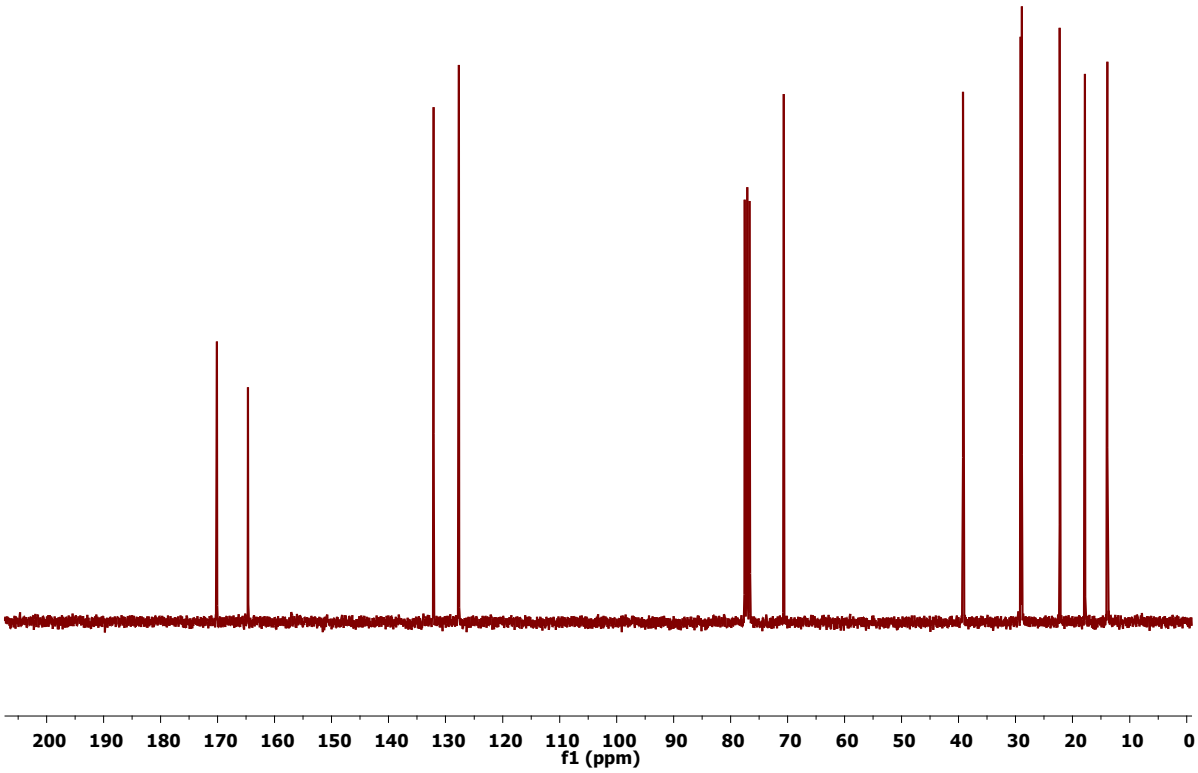


The Passerini 3-CR of acrylic acid **1** (721 mg, 686 µL, 10.0 mmol), acetaldehyde **3e** (441 mg, 10.0 mmol) and 1-pentyl isocyanide **2c** (972 mg, 1.26 mL, 10.0 mmol) in dichloromethane led to the formation of 1-oxo-1-(pentylamino)propan-2-yl acrylate. After drying in high vacuum, **4g** was obtained as clear oily product (2.12 g, quant.). TLC R_f = 0.44 (*n*-hexane/ethyl acetate = 2:1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.89 (t, J = 6.7 Hz, 3 H, CH_3), 1.19-1.39 (m, 4H, 2 CH_2), 1.43-1.57 (m, 2H, CH_2), 1.50 (d, J = 6.8 Hz, 3 H, CH_3), 3.19-3.32 (m, 2 H, NCH_2), 5.29 (q, J = 6.8 Hz, 1 H, OCHCO), 5.93 (dd, J = 10.2, 0.8 Hz, 1 H, C**H**$_2$CHCO), 6.02-6.14 (m, 1H, NH), 6.18 (dd, J = 17.3, 10.4 Hz, 1 H, CH_2C**H**CO), 6.49 (dd, J = 17.3, 0.9 Hz, 1 H, C**H**$_2$CHCO); ^{13}C NMR ($CDCl_3$, 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 $C_{11}H_{19}NO_3$ (M^+ = 213.2); HRMS (EI) of $C_{11}H_{19}NO_3$ $[M]^+$ calc. 213.1365, found 213.1363; IR (KBr) ν = 3303.6, 3098.3, 2958.0, 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}.

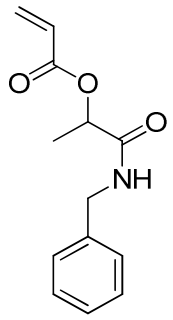
1H-NMR (CDCl3, 300 MHz)



13C-NMR (CDCl3, 75 MHz)

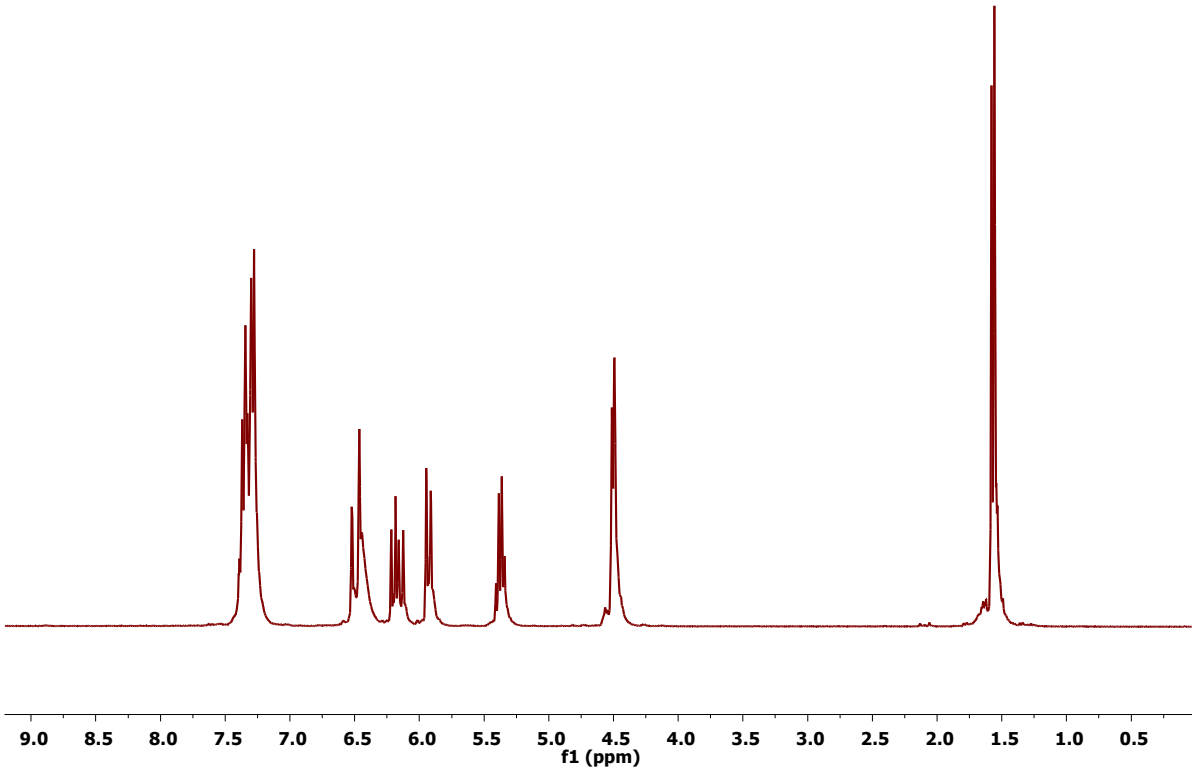


1.2.8 1-(Benzylamino)-1-oxopropan-2-yl acrylate (4h)

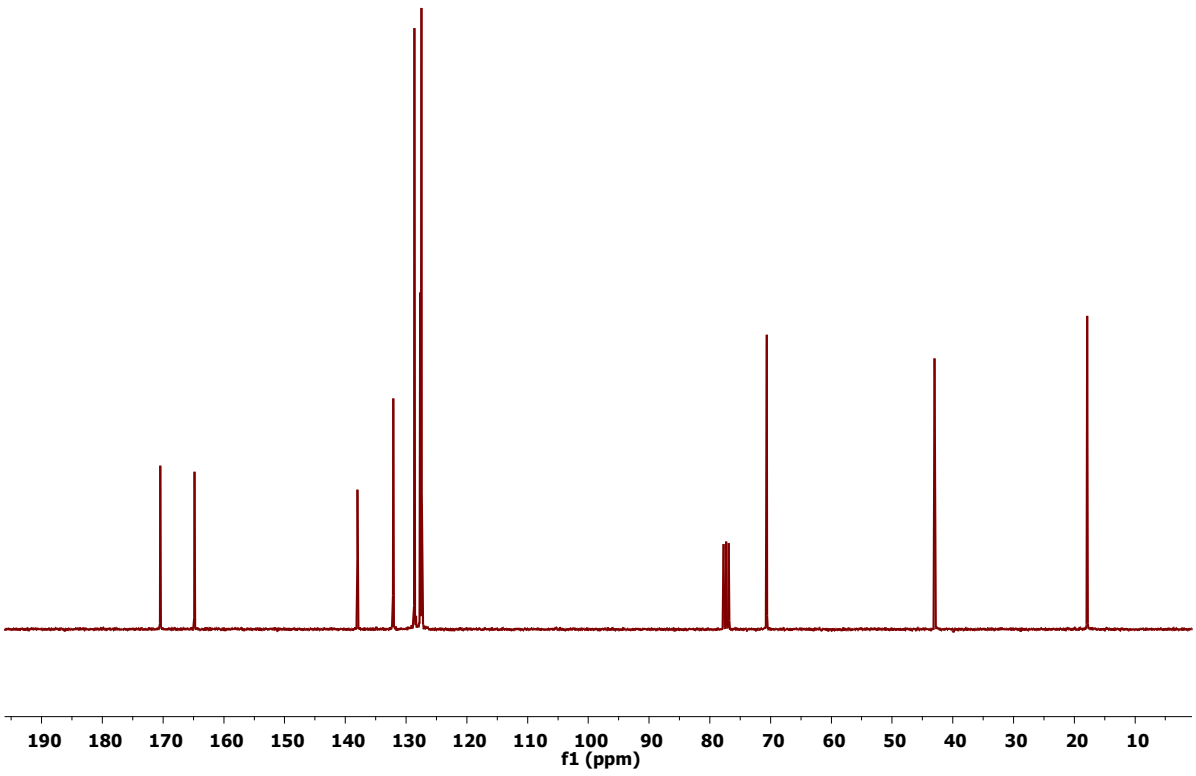


The Passerini 3-CR of acrylic acid **1** (721 mg, 686 µL, 10.0 mmol), acetaldehyde **3e** (441 mg, 10.0 mmol) and benzyl isocyanide **2d** (1.17 g, 1.22 mL, 10.0 mmol) in dichloromethane led to the formation of 1-(benzylamino)-1-oxopropan-2-yl acrylate. After purification by column chromatography (*n*-hexane/ethyl 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): δ (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, C**H**$_2$CHCO), 6.15 (dd, J = 17.3, 10.2 Hz, 1 H, CH_2C**H**CO), 6.29-6.52 (m, 1H, NH), 6.47 (dd, J = 17.3, 0.9 Hz, 1 H, C**H**$_2$CHCO), 7.14-7.46 (m, 5 H, 5 Ar-H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ (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) ν = 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).

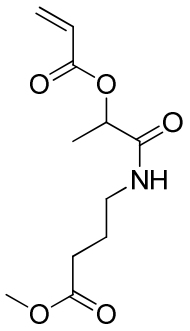
1H-NMR (CDCl3, 300 MHz)



13C-NMR (CDCl3, 75 MHz)

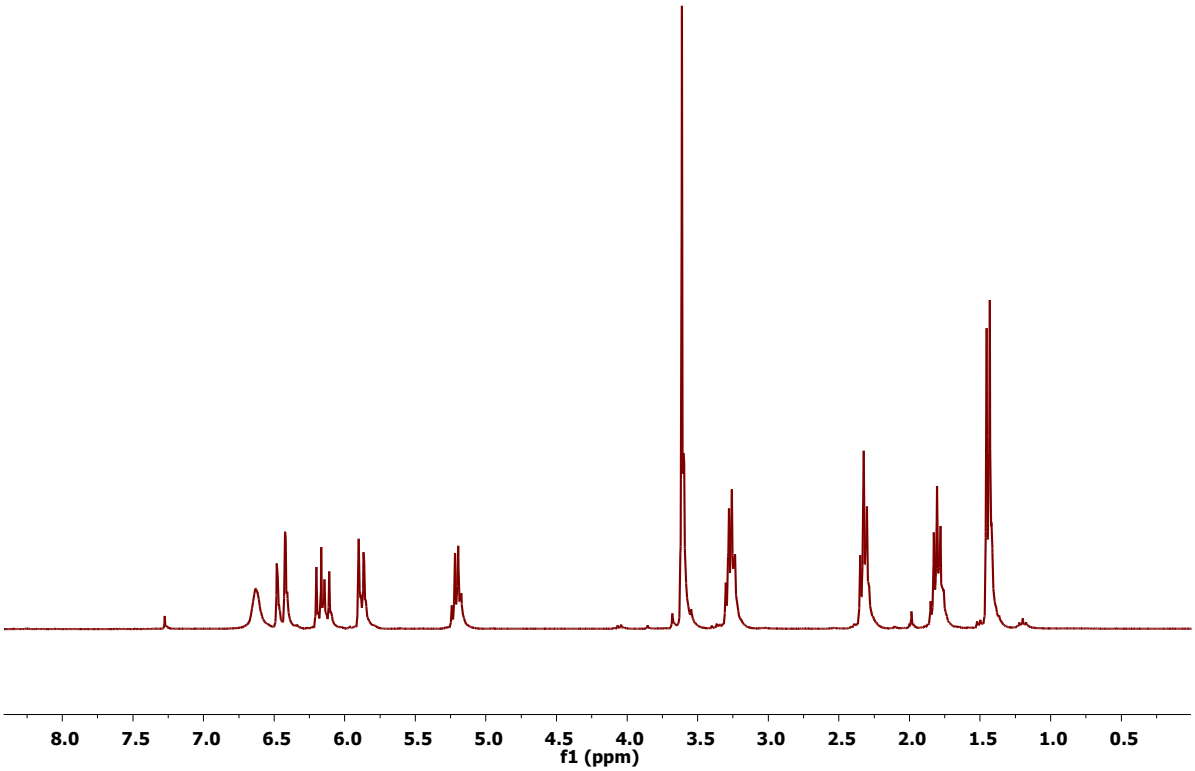


1.2.9 Methyl 4-(2-(acryloyloxy)propanamido)butanoate (4i)

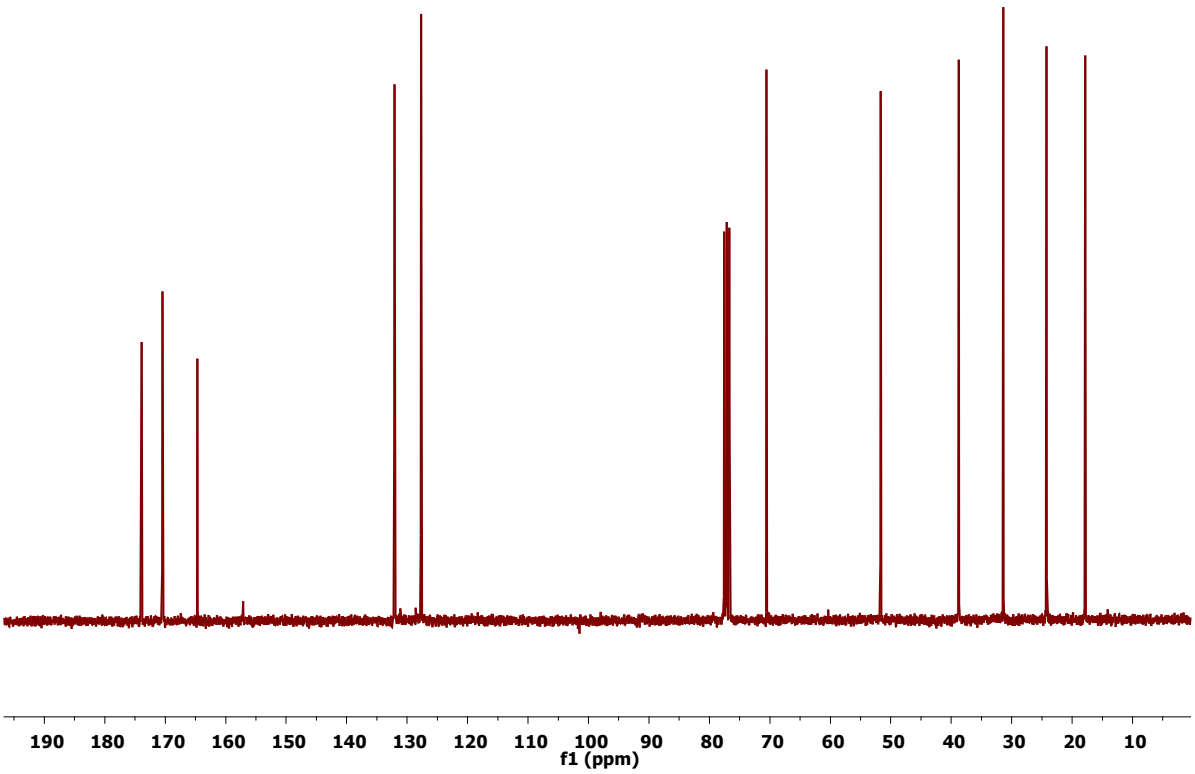


The Passerini 3-CR of acrylic acid **1** (721 mg, 686 µL, 10.0 mmol), acetaldehyde **3e** (441 mg, 10.0 mmol) and methyl 4-isocyanobutyrate **2e** (1.27 g, 10.0 mmol) in dichloromethane led to the formation of methyl 4-(2-(acryloyloxy)propanamido)butanoate. After purification by column chromatography (*n*-hexane/ethyl acetate 2:1), **4i** was obtained as a brown liquid (2.27 g, 94 %). TLC R_f = 0.17 (*n*-hexane/ethyl acetate = 2:1); ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.43 (d, J = 6.9 Hz, 3 H, CH_3),1.70-1.86 (m, 2 H, CH_2), 2.31 (t, J = 7.1 Hz, 2 H, $COCH_2$), 3.16-3.31 (m, 2 H, NCH_2), 3.60 (s, 3H, $COOCH_3$), 5.19 (q, J = 6.8 Hz, 1 H, OCHCO), 5.87 (dd, J = 10.4, 1.3 Hz, 1 H, C**H**$_2$CHCO), 6.14 (dd, J = 17.3, 10.4 Hz, 1 H, CH_2C**H**CO), 6.44 (dd, J = 17.3, 1.3 Hz, 1 H, C**H**$_2$CHCO), 6.49-6.74 (m, 1H, NH); ^{13}C NMR ($CDCl_3$, 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 $C_{11}H_{17}NO_5$ ($M+H^+$ = 244.1); HRMS (FAB) of $C_{11}H_{17}NO_5$ $[M+H]^+$ 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^{-1}.

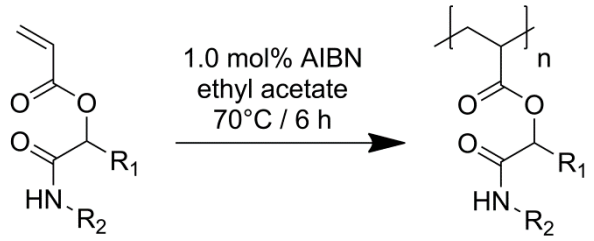
1H-NMR (CDCl3, 300 MHz)



13C-NMR (CDCl3, 75 MHz)



1.3 Free radical polymerization



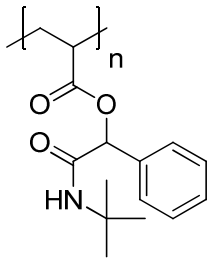
4a-4i **P1-P9**

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

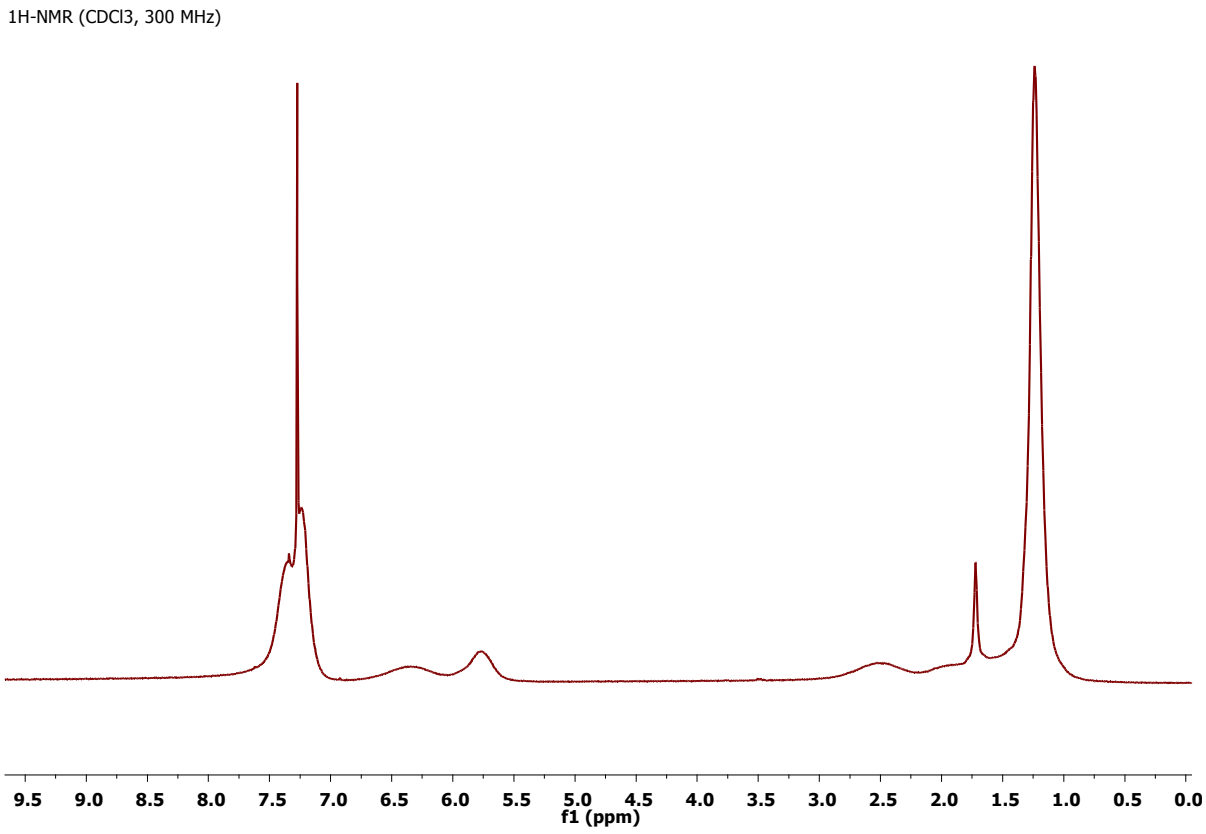
General procedure:

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.

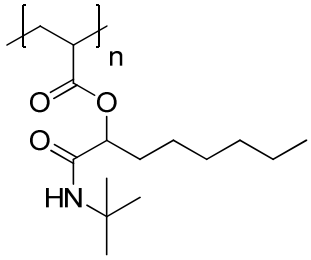
1.3.1 Polyacrylate derived from monomer 4a (P1)



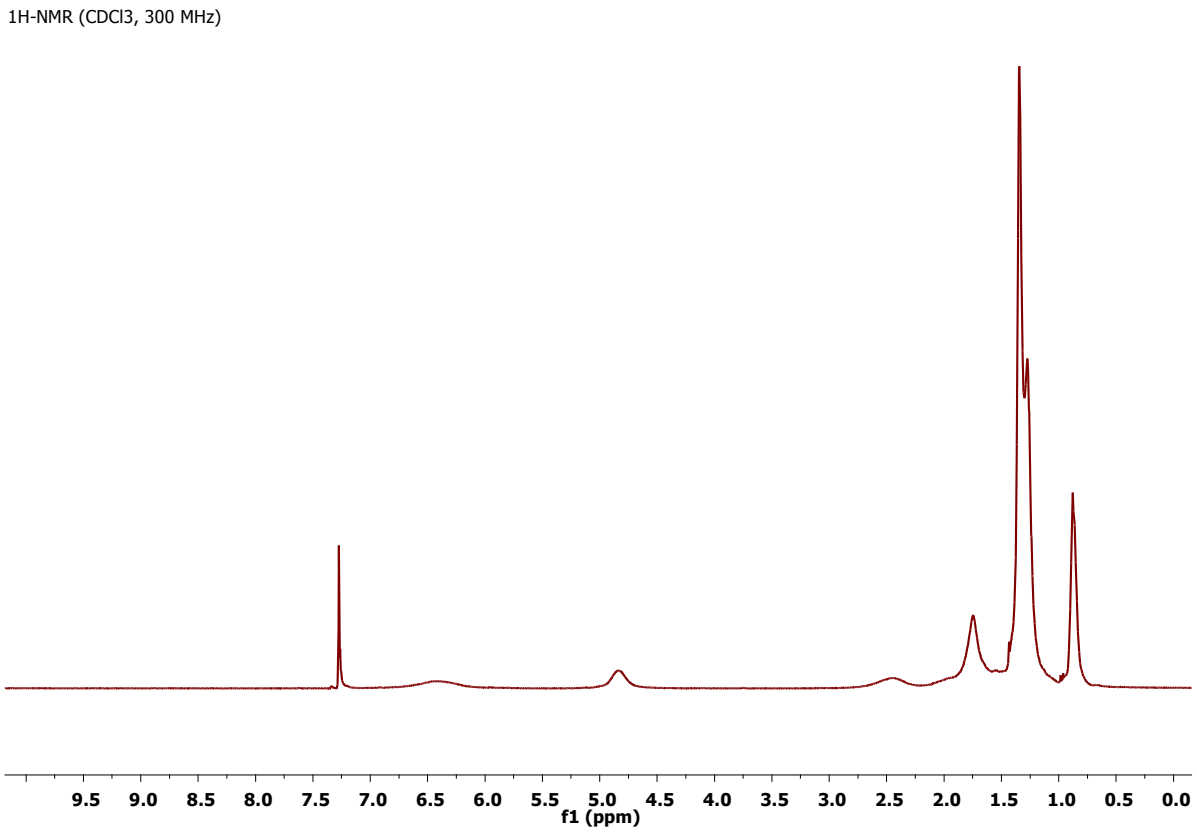
The free radical polymerization of monomer **4a** (523 mg, 2.00 mmol) yielded polyacrylate **P1** as colorless solid (392 mg, 75 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) = 1.22 (s, 9 H, 3 CH_3), 1.41-2.19 (m, 2 H, CH_2 backbone), 2.19-3.03 (m, 1 H, CH backbone), 5.47-6.00 (m, 1 H, OCHCO), 6.00-6.76 (br, 1 H, NH), 7.00-7.79 (m, 5 H, Ar-H); T_g = 123°C.



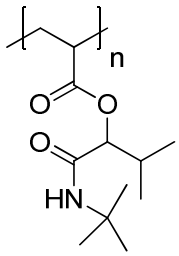
1.3.2 Polyacrylate derived from monomer 4b (P2)



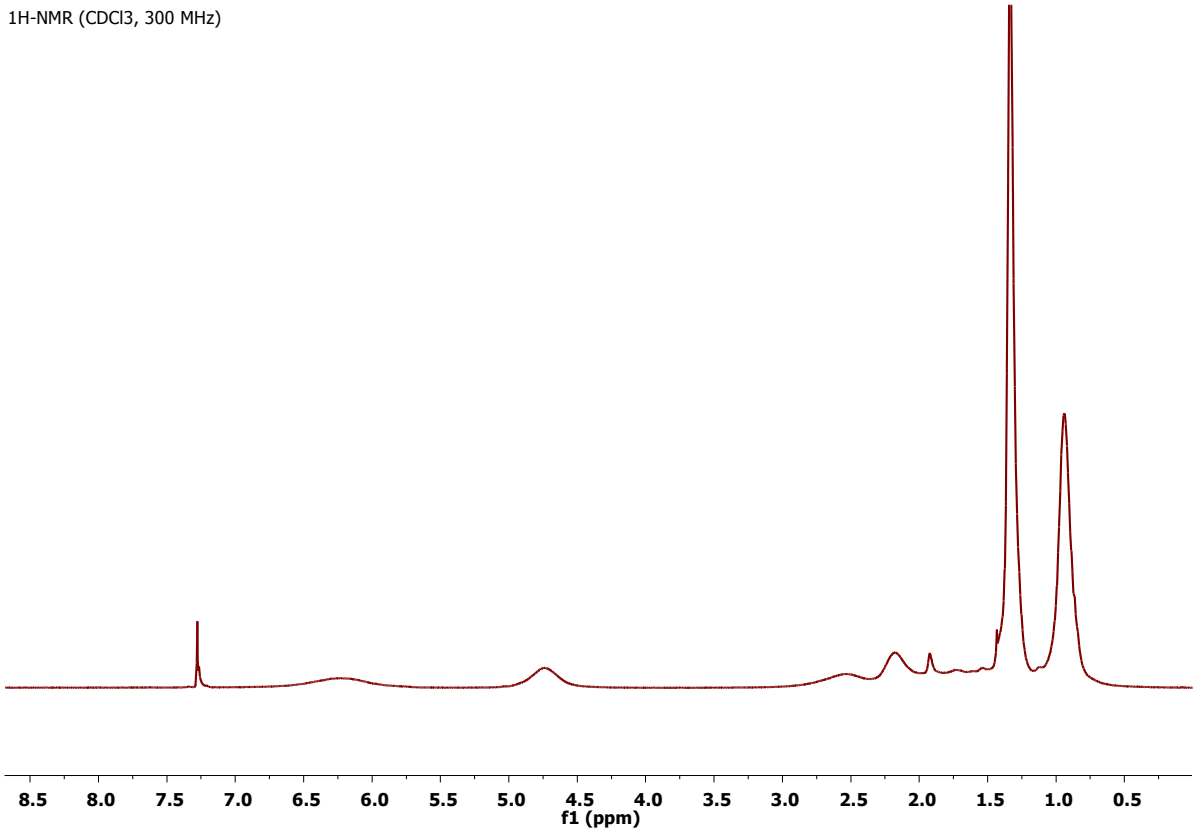
The free radical polymerization of monomer **4b** (539 mg, 2.00 mmol) yielded polyacrylate **P2** as colorless solid (423 mg, 79 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.72-1.00 (m, 3 H, CH_3), 1.00-2.15 (m, 12 H, 5 CH_2 and CH_2 backbone), 1.33 (s, 9 H, 3 CH_3), 2.15-2.87 (m, 1 H, CH backbone), 4.47-5.18 (m, 1 H, OCHCO), 5.90-6.92 (br, 1 H, NH); T_g = 59°C.



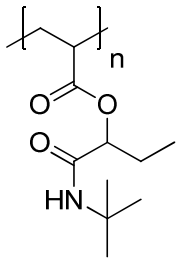
1.3.3 Polyacrylate derived from monomer 4c (P3)



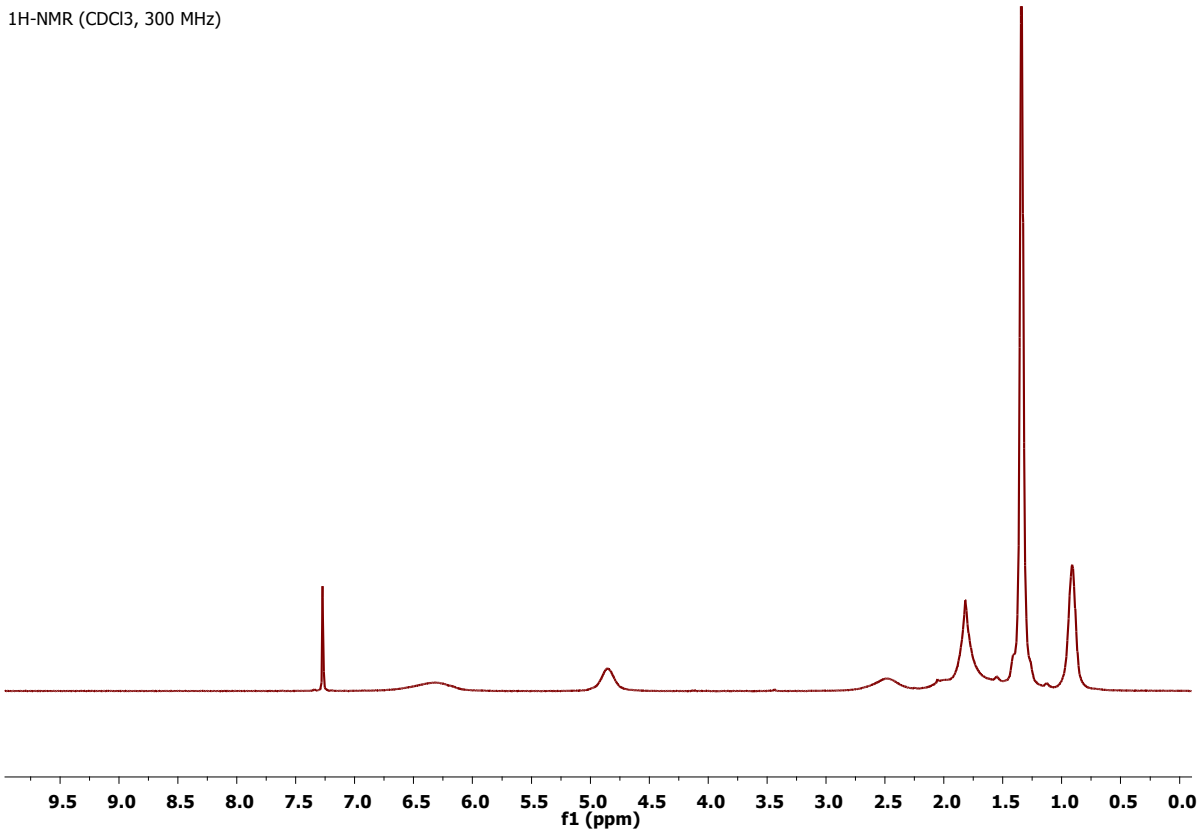
The free radical polymerization of monomer **4c** (455 mg, 2.00 mmol) yielded polyacrylate **P3** as colorless solid (337 mg, 74 %).^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.72-1.10 (m, 6 H, 2 CH_3), 1.32 (s, 9 H, 3 CH_3), 1.51-2.89 (m, 4 H, $CH(CH_3)_2$, CH_2 and CH backbone), 4.27-5.09 (m, 1 H, OCHCO), 5.68-6.82 (br, 1 H, NH); T_g = 111°C.



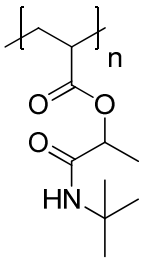
1.3.4 Polyacrylate derived from monomer 4d (P4)



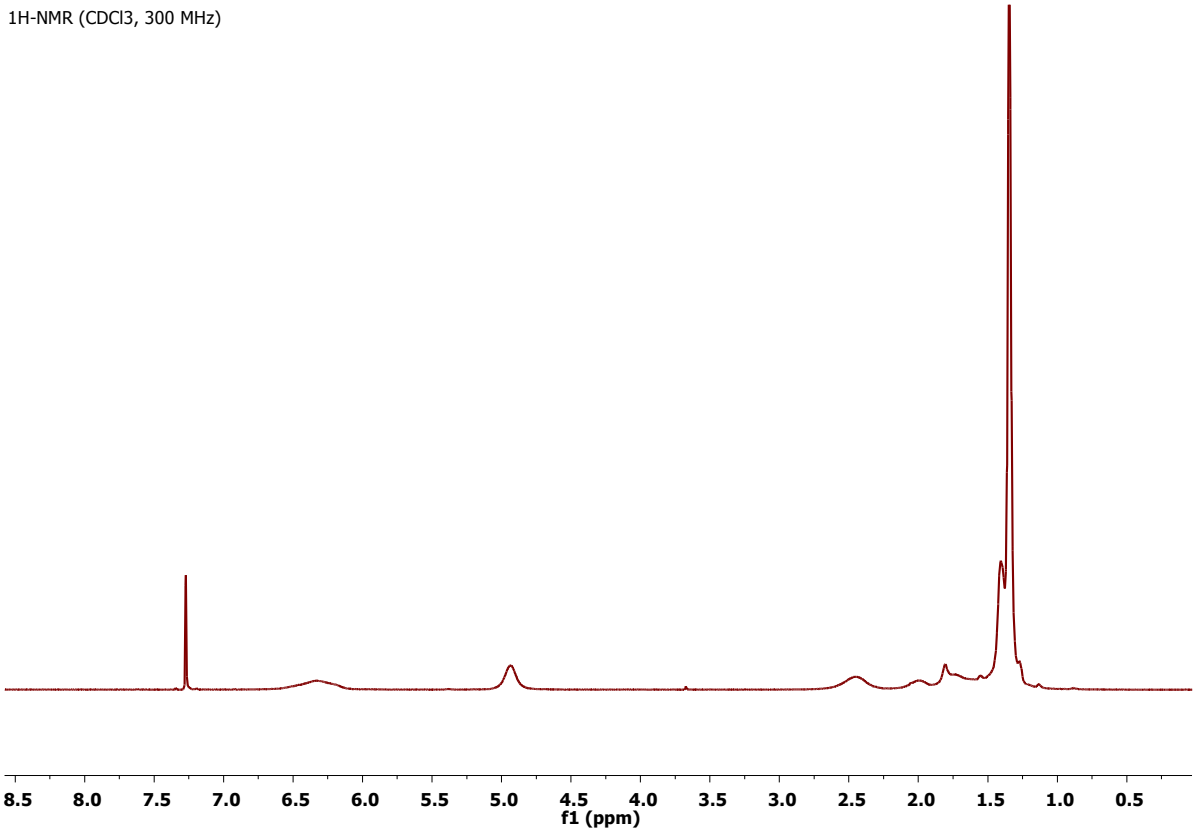
The free radical polymerization of monomer **4d** (427 mg, 2.00 mmol) yielded polyacrylate **P4** as colorless solid (278 mg, 65 %).^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.78-1.01 (m, 3 H, CH_3), 1.33 (s, 9 H, 3 CH_3), 1.48-2.12 (m, 4 H, CH_2, CH_2 backbone), 2.21-2.88 (m, 1 H, CH backbone), 4.57-5.10 (m, 1 H, OCHCO), 5.97-6.89 (br, 1 H, NH); T_g = 96°C.



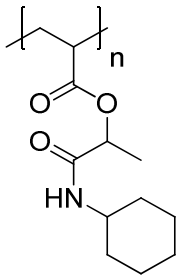
1.3.5 Polyacrylate derived from monomer 4e (P5)



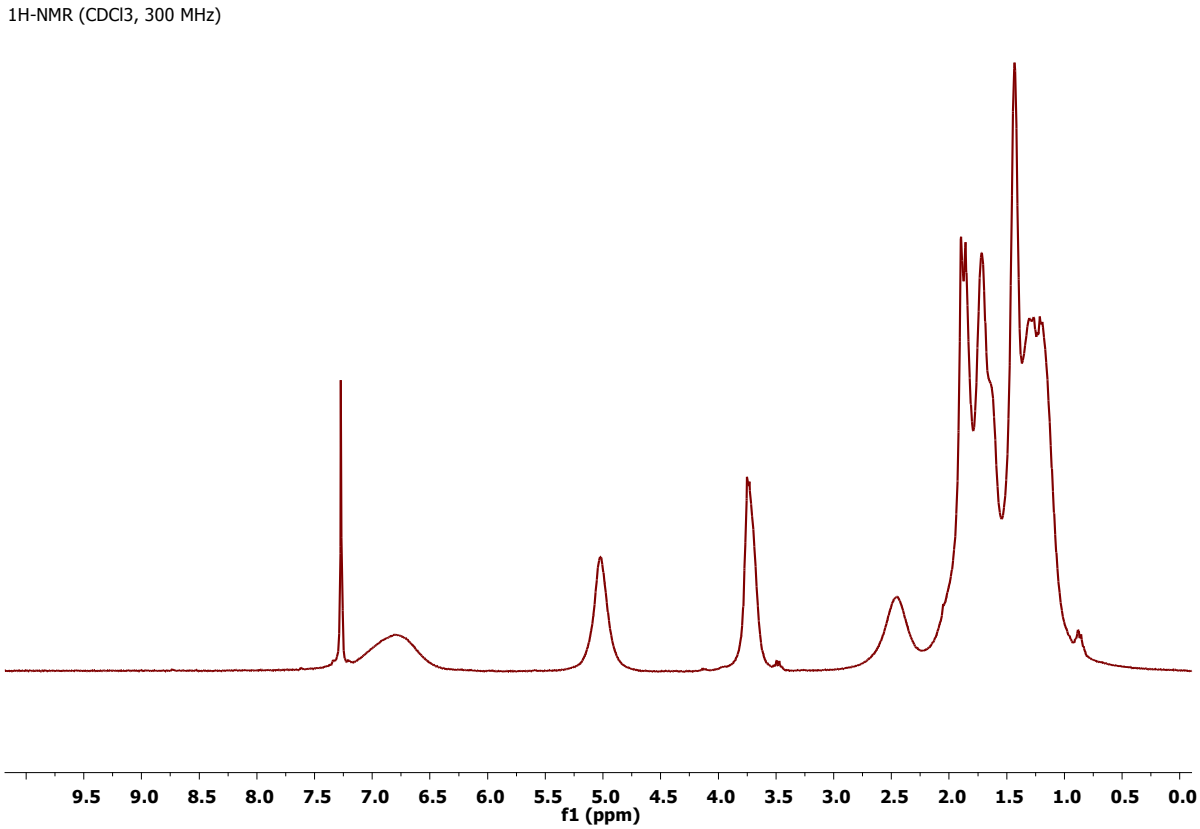
The free radical polymerization of monomer **4e** (399 mg, 2.00 mmol) yielded polyacrylate **P5** as colorless solid (266 mg, 67 %). ^{1}H NMR (CDCl3, 300 MHz): δ (ppm) = 1.33 (s, 9 H, 3 CH3), 1.35-1.45 (m, 3 H, CH3), 1.58-2.15 (m, 2 H, CH2 backbone), 2.20-2.69 (m, 1 H, CH backbone), 4.69-5.08 (m, 1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



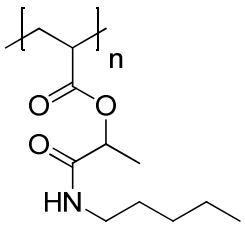
1.3.6 Polyacrylate derived from monomer 4f (P6)



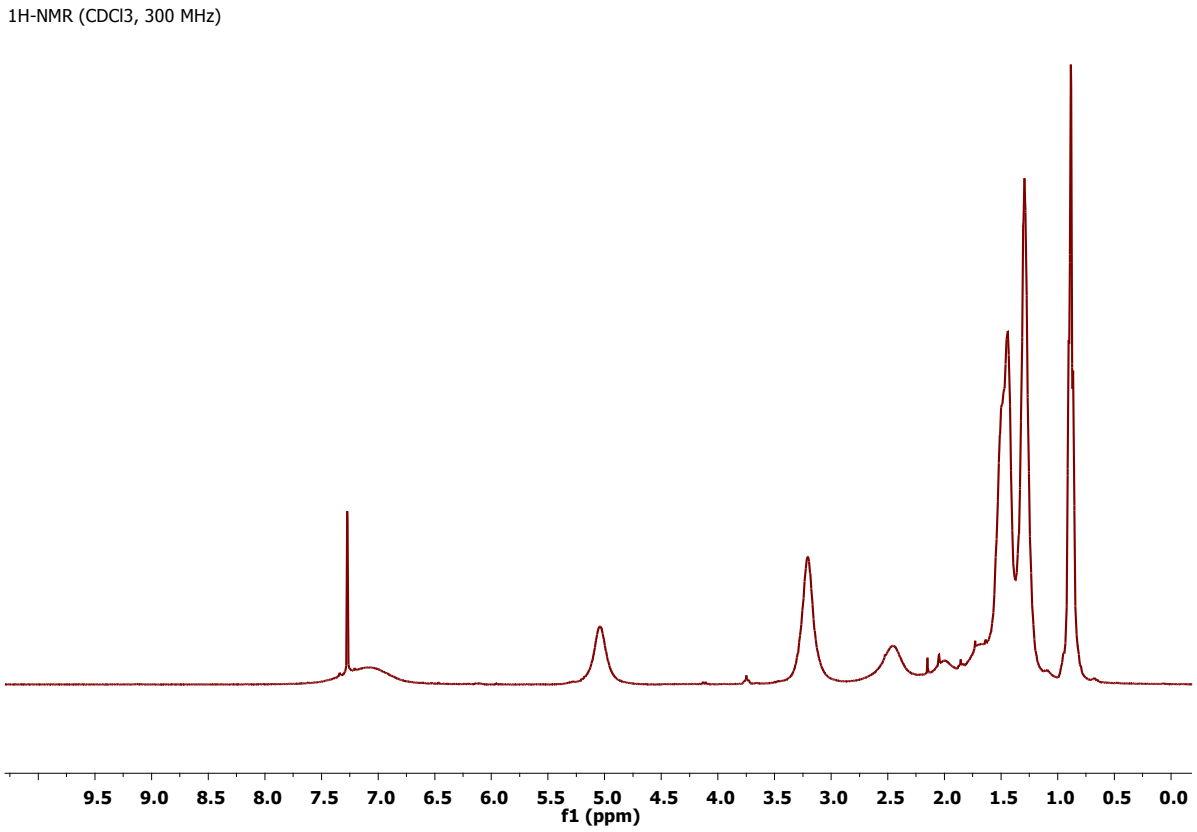
The free radical polymerization of monomer **4f** (451 mg, 2.00 mmol) yielded polyacrylate **P6** as colorless solid (387 mg, 86 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.85-2.21 (m, 12 H, 5 CH_2 and CH_2 backbone), 1.42 (m, 3 H, CH_3), 2.21-2.82 (m, 1 H, CH backbone), 3.53-3.96 (m, 1 H, NCH), 4.73-5.23 (m, 1 H, OCHCO), 6.36-7.27 (m, 1H, NH); T_g = 122°C.



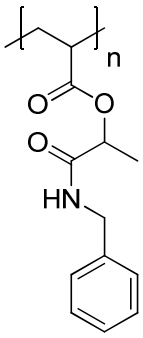
1.3.7 Polyacrylate derived from monomer 4g (P7)



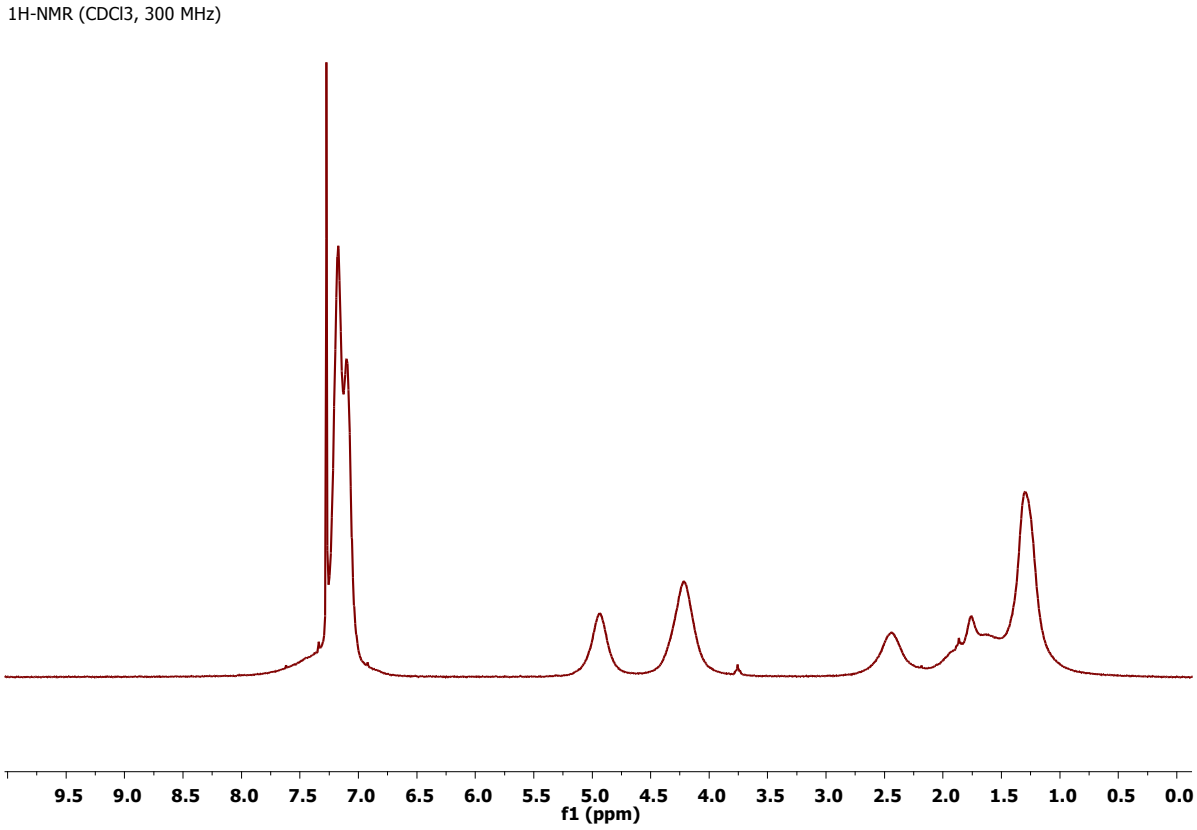
The free radical polymerization of monomer **4g** (427 mg, 2.00 mmol) yielded polyacrylate **P7** as colorless solid (345 mg, 81 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.87 (t, J = 5.9 Hz, 3 H, CH_3), 1.03-2.19 (m, 11 H, 3 CH_2, CH_3 and CH_2 backbone), 2.20-2.79 (m, 1 H, CH backbone), 2.87-3.49 (m, 2 H, NCH_2), 4.76-5.35 (m, 1 H, OCHCO), 6.60-7.55 (m, 1H, NH); T_g = 51°C.



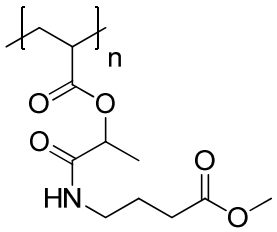
1.3.8 Polyacrylate derived from monomer 4h (P8)



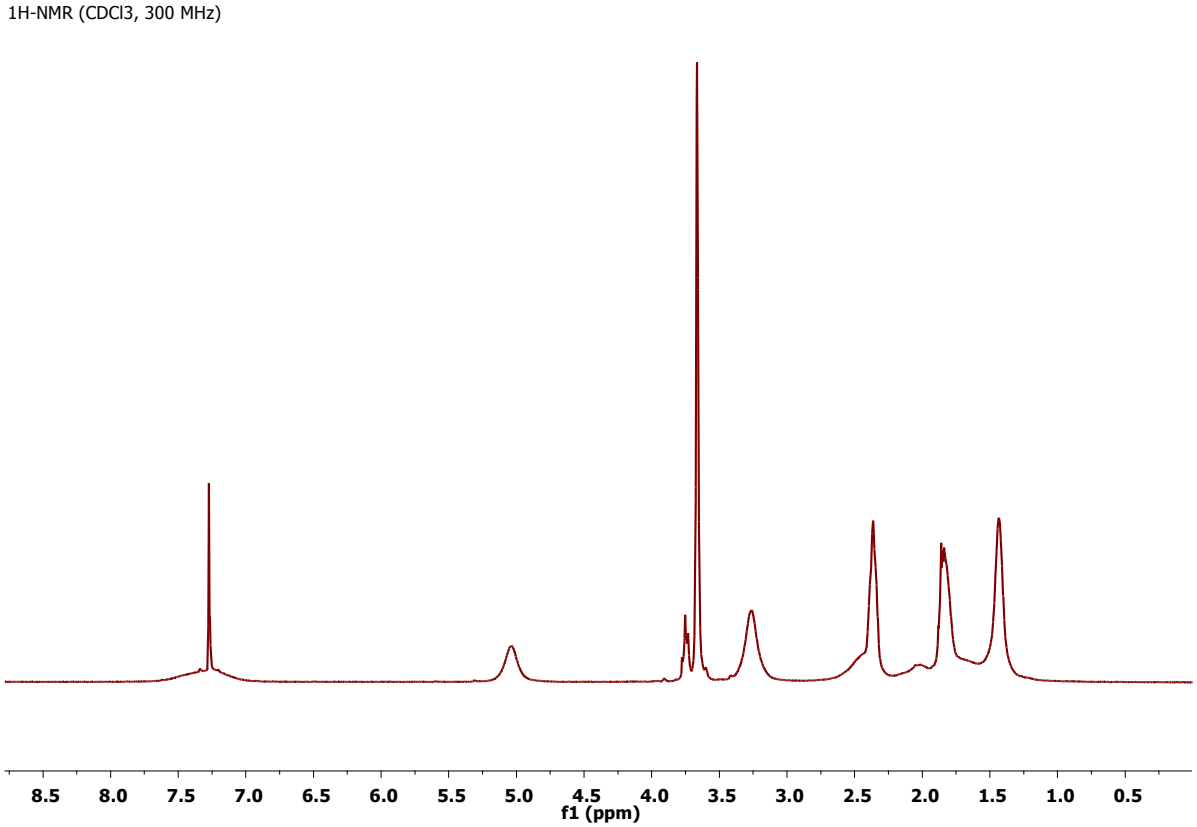
The free radical polymerization of monomer **4h** (467 mg, 2.00 mmol) yielded polyacrylate **P8** as colorless solid (352 mg, 75 %). ^{1}H NMR ($CDCl_3$, 300 MHz): δ (ppm) = 0.79-1.59 (m, 3 H, CH_3), 1.29-2.16 (m, 2 H, CH_2 backbone), 2.16-2.80 (m, 1 H, CH backbone), 3.86-4.49 (m, 2 H, NCH_2), 4.64-5.21 (m, 1 H, OCHCO), 6.73-7.80 (m, 6 H, NH and 5 Ar-H); T_g = 85°C.



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): δ (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_2COO), 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°C.



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

[i] Two-step procedure for the synthesis of isocyanides from primary amines: (a) Ugi, I.; Fetzer, U.; Eholzer, U.; Knupfer H.; Offermann, K. *Angew. Chem. Int. Ed.* **1965**, *4*, 472–484. (b) Nunami, K.; Suzuki I. M.; Yoneda, N. *Synthesis* **1978**, 840–841. (c) Obrecht, R.; Herrmann R.; Ugi, I. *Synthesis* **1985**, 400–402.

[ii] (a) Kreye, O.; Türünç, O.; Sehlinger, A.; Rackwitz, J.; Meier, M. A. R. *Chem.–Eur. J.* **2011**, *18*, 5767–5776. (b) Wessjohann, L. A; Henze, M.; Kreye, O.; Rivera, D. G. *WO Patent* 134,607, **2011**; *European Patent* 2563847, **2013**.