Melt-polymerization of acrylamide initiated by nucleophiles: a route towards highly branched and amorphous polyamide 3

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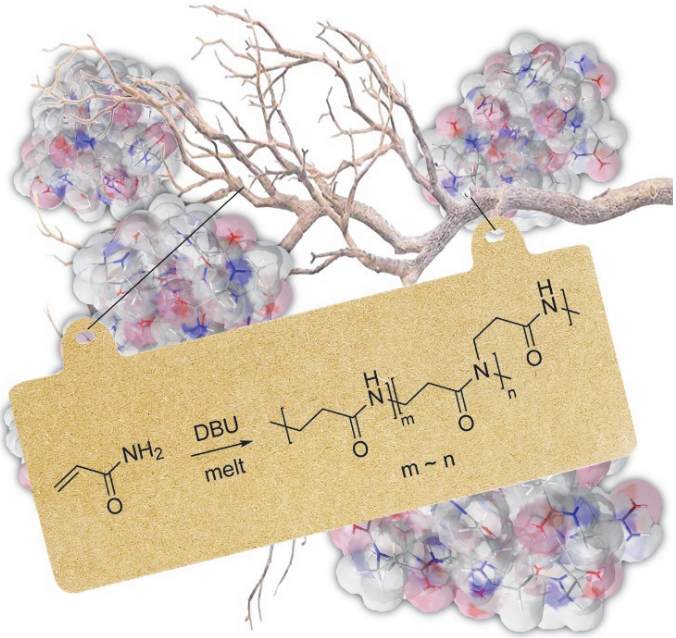


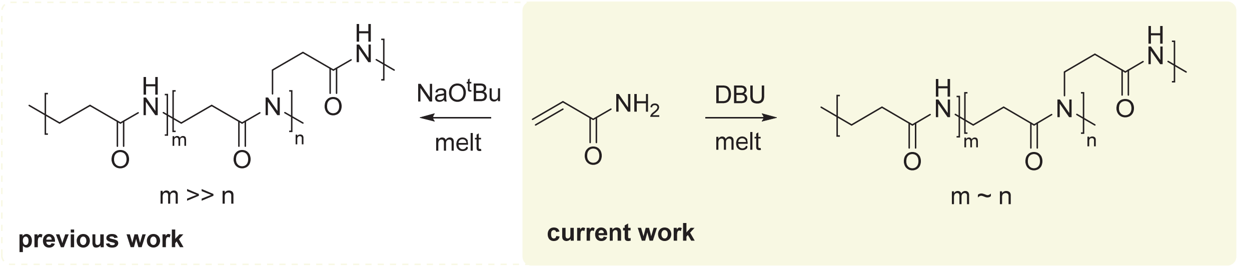
ABSTRACT: The melt-polymerization of acrylamide initiated by nucleophiles allows for the preparation of polyamide 3 (PA 3) with a branching factor of about 1.5. The high share of branching units imparts a fully amorphous morphology featuring a low glass transition temperature of 67 °C and renders the polymer water soluble. The disclosed method provides an easy, resource-efficient and green access to a polymer interesting for applications in biological and biomedical systems. The obtained PA 3 was characterized by several NMR-techniques, MALDI-TOF mass spectrometry, size-exclusion chromatography, thermal analyses and powder-X-ray diffractometry. Preparation and characterization of a ^{15}N-marked polymer complemented the elucidation of the polymers structure. Mechanistically, the polymerization can be considered as an *aza*-Michael polymerization of acrylamide involving zwitter-ionic species as the key intermediates being responsible for the high degree of branching.

Introduction

Polyamides (PAs) are a commercially important class of polymers with applications in many industries. Their utility primarily arises from the amide groups and hydrogen bonding among them, creating strong interchain interactions. These hydrogen bonding interactions are responsible for higher glass transition temperatures and melting points. Moreover, they are the main reason for the high strength and stiffness as well as the appealing friction and wear behavior of PAs compared to e.g. polyesters. For the same reason, most PAs are semi-crystalline, however, also amorphous representatives of this polymer class are known. In particular, amorphous partially aromatic PAs are of industrial relevance, since they combine transparency with excellent chemical resistance and thus compete with other transparent materials such as polycarbonates or poly(methylmethacrylate). The vast majority of PAs is prepared by either a condensation polymerization approach reacting diamines with dicarboxylic acid derivatives or by a chain grow process relying on ring-opening polymerization of cyclic amides.[1]

Polyamide-3 (PA 3), also named poly(β-alanine) or nylon-3, is a silk like PA characterized by a relatively high moisture absorption and high crystallinity. Linear PA 3 features a melting temperature of more than 320 °C and a glass transition temperature of more than 110 °C.[2,3,4,5,6] PA 3 can be prepared by ring opening of 2-azetidinone,[7,8] through catalytic ester–amide exchange,[9] via condensation polymerization of β-alanine in ionic liquids[10] or by *aza*-Michael polymerization of acrylamide also referred to as hydrogen transfer polymerization.[2-5,11,12,13] In the latter method usually strong bases are used as the initiators which leads to slightly branched PA 3 with a decreased crystallinity in comparison to perfectly linear PA 3. Nevertheless the polymerization of acrylamide following the protocol of Ross et al.[13] is appealing, because it is fast, cheap and resource saving. The preparation uses melted acrylamide and is initiated with low amounts of sodium *tert*-butoxide (NaO^{t}Bu). Thus, expensive and toxic solvents employed in heretofore-disclosed protocols are avoided.[2-5,11]

Scheme 1. Preparation of almost linear PA 3 from acrylamide (previous work) and highly branched PA 3 (this work).



Taking advantage of the reaction conditions disclosed by Ross et al., we herein disclose a protocol for obtaining fully amorphous PA 3 featuring a branching factor of about 1.5 in a melt polymerization approach. The preparation is solvent free in all stages and commercially available acrylamide is used. Exclusion of water or oxygen is not necessary. Thus, the reaction conditions are much more sustainable when compared to usually employed protocols for the synthesis of hyperbranched polymers.[14,15,16] In this case, the key for obtaining a high degree of branching is to use nucleophiles for initiating the polymerization. By nucleophilic initiation the reaction can be kept at the lowest possible temperature and zwitter-ionic species, which play a crucial role in favoring branched over linear growth, are formed. The use of nucleophiles for initiating the *aza*-Michael self-polymerization of acrylamide itself is not unprecedented. A single publication mentioning the use of sodium azide as initiator is available. In this work, Kumar et al. performed azide/alkyne click reactions with azide terminated PA 3 strands. Although they have not diligently discussed the consequences of using sodium azide as initiator for the architecture of the resulting PA 3 chains, they noted the presence of branching.[12] The herein disclosed branched PA 3 is easily water-soluble and might be applicable in biological and biomedical systems.[16,17]

Results and Discussion

Initially several nucleophiles were tested as initiators for the polymerization of acrylamide. For this purpose, acrylamide was melted and kept at a temperature of 83 °C under stirring. Then 2 mol% of the respective nucleophile was added. Sodium *tert*-butoxide (NaO^tBu) served as a base catalyst for comparison. The reaction vessel was closed and the reaction mixture was stirred for 24 h. Afterwards an aliquot of the reaction product was analyzed by NMR spectroscopy and the conversion of the acrylic double bond and the ratio between linear and branched repeat units was determined (vide infra). Results are gathered in Table 1. Relatively weak nucleophiles (judged by their methyl cation affinity (MCA)[18]) such as 1,4-diazabicyclo[2.2.2]octane (DABCO) and trimethylamine (NEt_3) are not suited to promote the reaction under these conditions. DABCO gave only approx. 37 % double bond conversion and NEt_3 showed no reactivity at all (Table 1, entries 1 and 2). By using the more nucleophilic 4-dimethylaminopyridine (DMAP) the double bond conversion was higher, reaching 90 %. In contrast to the reaction catalyzed by the non-nucleophilic base NaO^tBu, a high branching ratio of about 63 % was obtained (Table 1, entries 3 and 6). Using 1,8-diazabicyclo[5.4.0]undec-7-en (DBU) featuring a higher MCA than DMAP gave almost full double bond conversion and a branching ratio of about 50 % (Table 1, entry 4). A similar branching was obtained by employing triphenylphosphine (PPh_3), however, at a rather moderate double bond conversion of below 90 %.

Table 1. Initiator/catalyst screening for the polymerization of acrylamide (**1**)[a]

Entry	**Initiator**	**MCA [18] [kJ/mol]**	**pK_a [19,b]**	**Loading [mol%]**	**Conversion [%][c]**	**Branching ratio n/m [%][d]**
1	DABCO	562.2	8.16	2	37±1	n.d.[e]
2	NEt_3	562.3	10.26	2	0	n.d.
3	DMAP	581.2	8.27	2	89±1	61±4[e]
4	DBU	609.6	11.02	2	>99	51±2
5	PPh_3	618.7	1.31	2	87±1	50±2[e]
6	NaO^tBu	-	15.72	2	98±1	5±1
7	DMAP	581.2	8.27	1	78±1	n.d.[e]
8	DBU	609.6	11.02	1	>99	50±2
9	DBU	609.6	11.02	0.5	>99	52±2
10[f]	DBU	609.6	11.02	0.1	97±1	55±2

[a] reaction conditions: 1 g of **1**, solvent free, 83 °C oil bath temperature, 24 h. [b] pK_a of the conjugated acid calculated using the pK_a prediction platform (neural network result for solvent H_2O) available at pka.luo-group.com. [c] double bond conversion calculated using the integration of the respective ^1H-NMR spectrum in D_2O at 25 °C according to $(\text{integral}_{3.95\text{-}3.22}/2)/((\text{integral}_{3.95\text{-}3.22}/2)+(\text{integral}_{5.89\text{-}5.63}))\cdot 100$. [d] branching ratio (branched repeat units / linear repeat units) calculated using the integration of the respective ^1H-NMR spectrum in D_2O at 25 °C according to $(\text{integral}_{3.95\text{-}3.44}/2)/((\text{integral}_{3.95\text{-}3.44}/2)+(\text{integral}_{3.44\text{-}3.22}))\cdot 100$. [e] high share of di- and trimers present; [f] prepared at 90 °C oil bath temperature.

This result might be best explained by the low solubility of PPh_3 in the melt. It is conceivable, that only minor amounts of initiator became active. Due to their high double bond conversion, DMAP and DBU were further investigated using lower initiator loadings. With 1 mol% DMAP the double bond conversion dropped to about 78 % (Table 1, entry 7). In contrast, the DBU loading could be reduced to 0.5 mol% without changing the double bond conversion or the branching significantly. Using 0.1 mol% DBU a reaction temperature of 90 °C was needed to obtain a conversion above 96 % in 24 h (Table 1, entry 10). All branched products are well soluble in water or DMSO, while the mostly linear PA 3 retrieved from entry 6 is soluble in water but only sparingly soluble in DMSO.

The ^{1}H-NMR spectrum of PA 3 gives rise to two groups of signals (Fig. 1). The first signal group is located between 2.9 and 2.3 ppm and can be assigned to the methylene group attached to the carbonyl. The peak accumulation between 3.9 and 3.2 ppm can be assigned to the methylene group next to nitrogen. Linear repeat units give rise to much sharper signals at 2.4 and 3.4 ppm as revealed by the ^{1}H-NMR spectrum of PA 3 prepared with NaO^{t}Bu. The anticipated terminal vinyl group is hardly observed in samples prepared with DBU (Fig. 1c). Integration of the signals in the range of 3.9 to approx. 3.4 ppm (chemical shifts are slightly concentration dependent) and 3.4 to 3.2 ppm allows for an estimation of the ratio of branched to linear repeat units.

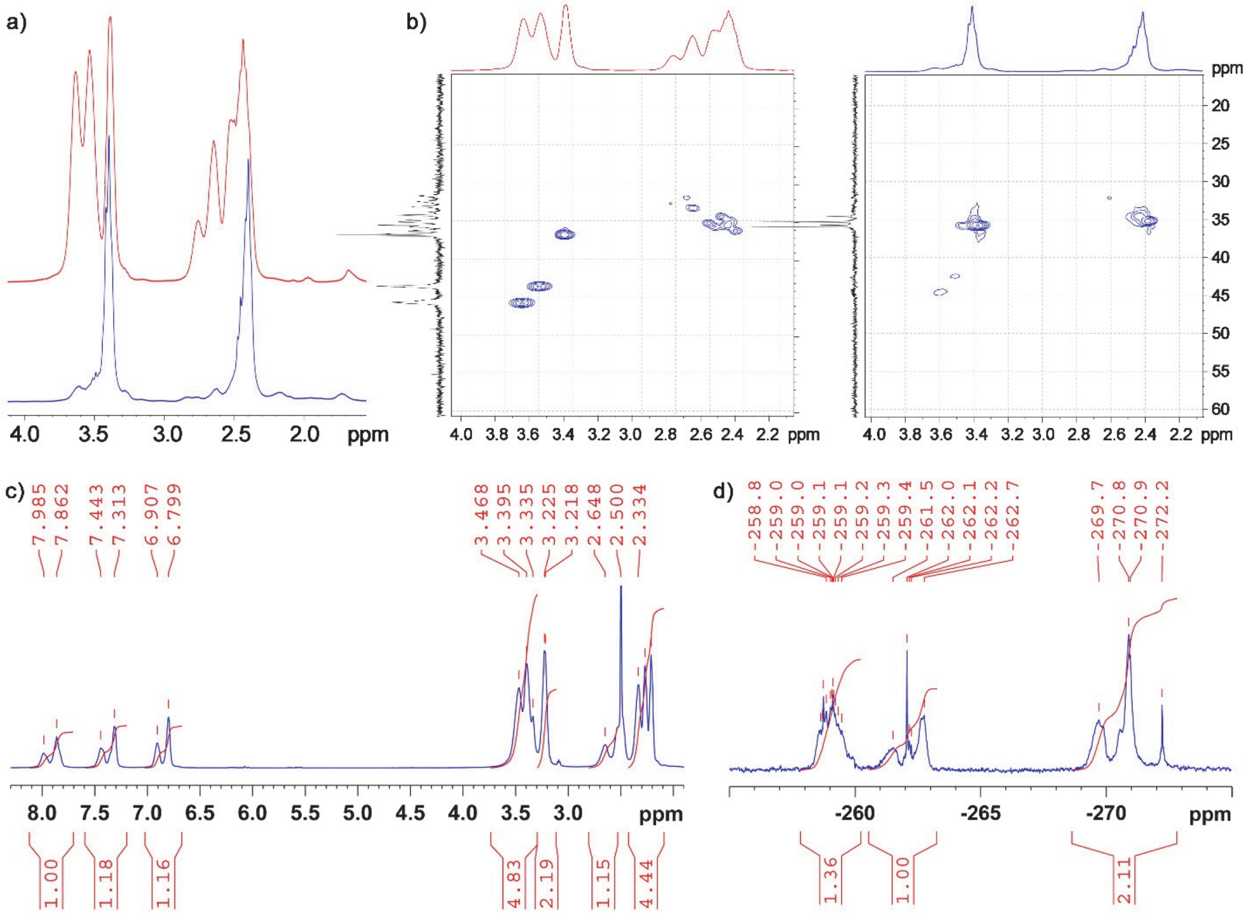


Figure 1. a) ^{1}H-NMR spectra in D_2O; red: PA 3 prepared with 2 mol% DBU (Table 1, entry 4); blue: prepared with 2 mol% NaO^{t}Bu (Table 1, entry 6). b) Heteronuclear Single Quantum Coherence (HSQC) spectra in D_2O of PA 3 prepared with 2 mol% DBU (Table 1, entry 4); blue: prepared with 2 mol% NaO^{t}Bu (Table 1, entry 6). c) ^{1}H-NMR spectrum in DMSO-d_6 of PA 3 prepared with 1 mol% DBU (Table 1, entry 8). d) ^{15}N{^{1}H}-NMR spectrum of ^{15}N-PA 3 prepared with 2 mol% DBU.

In the ^{13}C-NMR spectra linear repeat units give rise to signals at 174.6 (amide carbon) and 36.8-35.4 ppm representing both methylene-carbons. Branched units show the amides carbons at about 177 ppm and feature peaks at 45.5 and 43.4 assigned to the methylene carbons attached to a tertiary amid nitrogen. The signals for the other methylene carbons exhibit a higher chemical shift distribution (36.7-31.5 ppm). J-modulated spin-echo (JMOD) ^{13}C-NMR spectra of PA 3 prepared with 2, 1 and 0.5 mol% DBU showed no tertiary carbon atoms indicative for vinyl-type polymerized acrylamide. By recording the ^{1}H-NMR spectra in DMSO-d_6 the protons attached to nitrogen atoms can be observed. Thus, upon integration, the ratio of secondary (8.00 and 7.86 ppm) to primary amide groups (7.44, 7.31 and 6.91, 6.80 ppm) can be determined. PA 3 prepared with 1 mol% DBU showed a 1 : 1.17 ± 0.05 ratio of secondary to primary amide protons. The assignment of the protons and the validity of the calculations were checked by preparing ^{15}N-labeled PA 3. In this case, a double bond conversion of 92% was obtained. In the corresponding ^{15}N-NMR spectrum, three signal groups from -257.7 to -258.8 (*tert*-amide), -261.0 to -262.8 (*sec*-amide) and -269.4 to -272.0 ppm (*prim*-amide; all chemical shifts relative to ^{15}N-nitromethane) were observed. The assignment was made on basis of the corresponding multiplicities of the proton coupled ^{15}N-NMR spectra (Fig. S18). Integration delivered a ratio of *tert*-amide : *sec*-amide : *prim*-amide = 1.35 : 1 : 2.14 and accordingly a branching ratio of 57.5% (values for the degree of branching according to Fréchet or Frey are given in the SI). The corresponding evaluation of the proton spectrum delivered similar results with a branching ratio of 61 % (1.56 : 1 : 2.09). The somewhat higher value for branching obtained from the ^{1}H-NMR spectrum is most probably due to a relatively high abundance of the dimer *N*-(3-amino-3-oxopropyl)acrylamide. In this compound, the methylene group next to the acrylamide-nitrogen atom is shifted downfield and overlaps with the region indicative for branching. In samples with almost complete double bond conversion, this complication becomes less important and branching ratios determined by integration of the ^{1}H-NMR spectrum can be considered reliable.

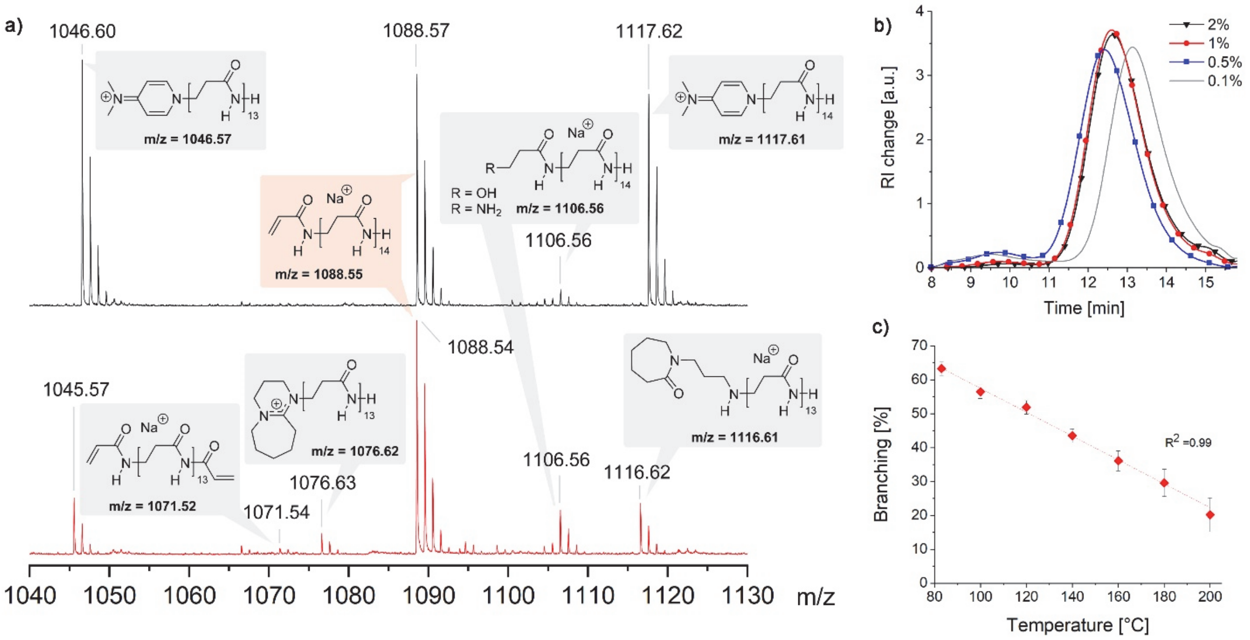


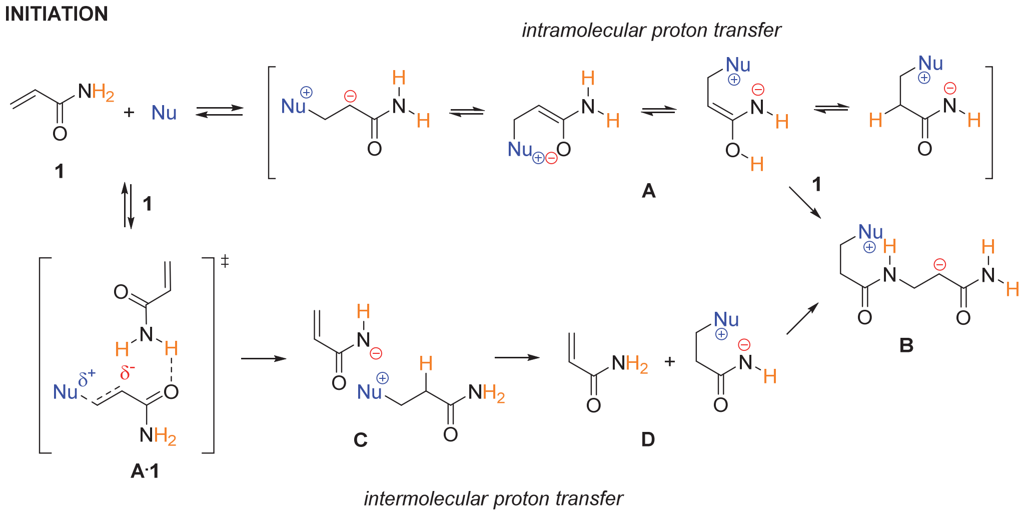
Figure 2. a) above: MALDI-TOF MS of PA 3 prepared with 2 mol% DMAP (Table 1, entry 3); below: MALDI-TOF MS of PA 3 prepared with 2 mol% DBU (Table 1, entry 4). b) Size-exclusion chromatograms of PA 3 prepared with 2, 1, 0.5 and 0.1% DBU (Table 1, entries 4, 8-10). c) branching ratio m/n in dependence of the reaction temperature.

PA 3 prepared with 2 mol% DMAP and with 2 mol% DBU were investigated with MALDI-TOF MS (Fig. 2, S19). The DMAP initiated sample exhibited two main series. The first one contains a DMAP moiety, most likely incorporated into PA 3 as the end-group. The second main series consist of only acrylamide repeat units only. Further, a minor series resulting from the formal reaction of the terminal acrylic double bond with either water or ammonia could be observed. The DBU initiated sample exhibited a single main series exclusively built up by acrylamide. Several minor series were observed, including a PA 3 series terminated with DBU or a PA 3 series terminated with a decomposition product of DBU.[20],[21] SEC-MALS investigations in DMSO (containing LiBr) were carried out to determine the absolute molar mass averages of branched PA 3 in dependence of the DBU loading. The molar mass averages increased with decreasing DBU content pointing to a chain-growth like mechanism of the polymerization. PA 3 prepared with 2 mol% DBU is characterized by a number average molar mass (M_n) of 6900 g/mol (dispersity Đ = 2.2, full data in Table S1), while samples prepared with 1 mol% or 0.5 mol% DBU revealed higher molar mass averages (M_n = 10800 g/mol; Đ = 1.8 and M_n = 23400 g/mol; Đ = 1.7, respectively). While the double bond conversion in the above-mentioned PA 3 samples was higher than 99 %, PA 3 prepared with 0.1 mol% DBU showed a double bond conversion of only 97 %. Not surprising, in this case, the molar mass averages are lower than anticipated (M_n = 9500 g/mol; Đ = 1.7). The chromatograms of all samples show the presence of a small amount of high molar mass species eluting between 8 and 11 min (Fig. 2). These species presumably result from intermolecular association of fully dissolved PA 3 molecules.

Ross et al. reported an increase of branching when lowering the amount of NaO^{t}Bu. At the same time, they noted a decrease of the reaction exothermy when lowering the amount of base.[11] When using DBU or DMAP instead of NaO^{t}Bu, only minor self-heating (1-2 °C) of the reaction mixture was observed. Accordingly, we hypothesized that the degree of branching of PA 3 can be influenced by adjusting the reaction temperature. To prove this assumption, PA 3 was prepared at various temperatures in a Monowave 50 reactor, which allows rapid heating of the samples. Several polymerizations were conducted at temperatures between 83 and 200 °C. PA 3 with a double bond conversion of 96±2 % was obtained in all cases (except for 83 °C, double bond conversion = 91±1 %). The degree of branching decreased linearly with increasing temperature (Fig. 2) reaching 20±5 % at 200 °C. At the same time, vinyl-type connectivity became more important (Fig. S20).

To understand this reaction a mechanistic rational needs to be developed answering particularly the two following questions: Why a nucleophile initiated reaction gives more branching than the base catalyzed version? What is the reason for obtaining higher molecular weights when decreasing the nucleophile amount? Let us first shed light on the initiation step. Here the nucleophile is reacting with **1** forming the zwitter-ion **A**, which can be formulated by several resonance structures (Scheme 2).

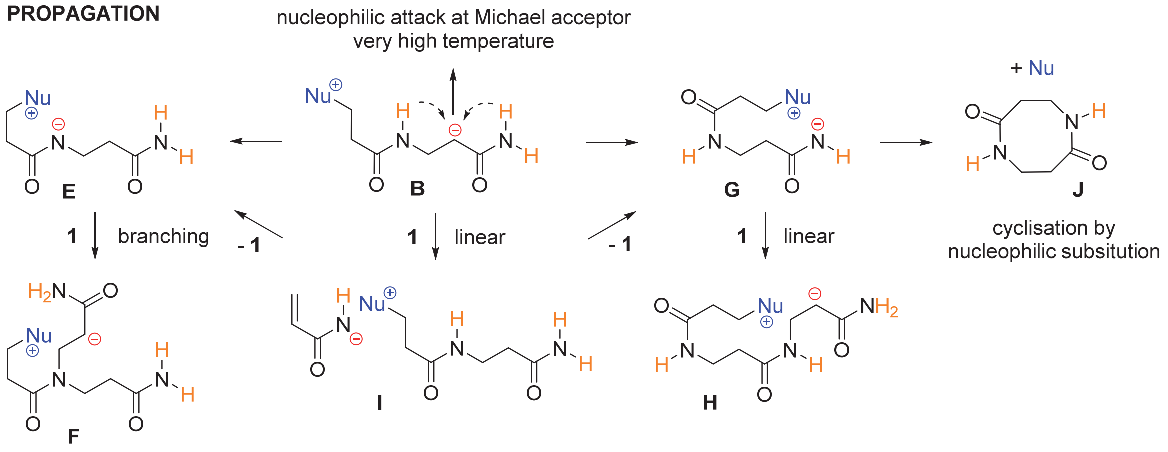
Scheme 2. Suggested mechanism for the initiation



The interconversion of the resonance structures involves proton transfer steps, which potentially result in the shift of the negative charge to the nitrogen atom. Subsequently the deprotonated nitrogen atom acts as nucleophile in an *aza*-Michael reaction with another molecule of **1** forming the dimer **B**. Alternatively, an intermolecular proton transfer from another acrylamide proceeding via a transition state **A·1** leading to the ion pair **C** might occur.

A similar pathway is believed to operate in the polymerization of acrylic acid,[22] in the *aza*-Michael reaction of amines with electron-deficient olefins[23,24,25] and in the *oxa*-Michael reaction of alcohols with divinyl sulfone.[26,27] Conversion of ion-pair **C** to the zwitterion **D** is likely because amide protons in **C** (calculated $pK_a = 8.8$, Nu = NMe_3) are much more acidic than those in **1** (calculated $pK_a = 12.9$, Fig. S22).[19] Eventually, **D** undergoes the *aza*-Michael reaction with another molecule of **1** forming the zwitter-ionic dimer **B**. Accordingly, the difference between base and nucleophile induced reaction pathways is the formation of zwitter-ionic species in the latter. This process is much slower than the direct deprotonation of **1** by a strong base. As the consequence, only minor amounts of anions are present and in contrast to the base promoted reaction, the reaction heat is released over a long period causing only marginal self-heating of the reaction mixture. In the next step, zwitter-ion **B** might rearrange via an intermolecular hydrogen transfer to yield either zwitter-ions **E** or **G** (Scheme 3)[11] and their reaction with a third molecule of **1** produces a branching point or leads to a linear elongation. It is easily conceivable that the *aza*-Michael reaction of **E** with **1** (or a higher analogue of **1** containing a Michael acceptor) leads to the creation of a branching point (like shown in **F**). Linear elongation could occur via zwitter-ion **G**. Alternatively, **B** might undergo an intermolecular hydrogen transfer with another abundant (or acidic) proton source such as **1**. The newly formed ion-pair **I** continues to react similarly as sketched for the initiation step, i.e. zwitter-ions **E** or **G** are formed (Scheme 3). Accordingly, it is plausible that the zwitter-ions like **E** are the key players for propagation at low temperatures where the highest branching degree is observed. Upon raising the temperature, propagation via **G** becomes more important.

Scheme 3. Suggested mechanism for branching during propagation



Raising the temperature even further, creation of vinyl-type connections via *carba*-Michael reactions of carbanionic structures like **B** becomes feasible.[11] Moreover, structures like **E** or **G** might also undergo nucleophilic substitution reactions at the carbon atom in α-position to the nucleophile leading to cyclic structures (such as **J**) or, in case of an intermolecular reaction, to an elongation of the chain (not shown).

As has been shown before, MALDI-TOF MS data provide evidence for the presence of nucleophile bearing macromolecules (Fig. 2). Additionally, NMR spectra of the DMAP initiated polymerization product at 83 °C suggest the presence of free as well as alkylated (and/or protonated) DMAP species. Upon raising the temperature to 100 °C and higher, the amount of free DMAP is distinctly increased (Fig. S20). The latter observation substantiates the occurrence of nucleophilic substitution reactions leading to **J** (and non-cyclic congeners). Accordingly, it is hypothesized that the generation of deprotonated secondary amides is thermodynamically preferred while deprotonated primary amides are kinetically favored. The relative stability of **E** over **G** is plausible because of the closer proximity of the positively and negatively charged moieties in **E**. Obviously such stabilization does not exist in the base catalyzed polymerization of **1**. Nevertheless also branched repeat units are generated in the base catalyzed case, albeit to a smaller extent. This suggests that the zwitter-ions are not necessary to obtain branching but zwitter-ions are promoting the branching. This hypothesis is supported by the observation that branching in the nucleophile initiated reaction is distinctly higher than in the base initiated variant conducted at the same temperature. Ross et al. reported a branching ratio of 11 % in the NaO^tBu initiated reaction reaching a maximum temperature of 160 °C.[11] In contrast, our DMAP initiated polymerization conducted at 160 °C gave about 35 % branching ratio. Sub-summarizing this section allows for answering the first question. Higher branching in case of nucleophilic initiation is obtained because self-heating is less pronounced and branching occurs preferably at low temperatures. Furthermore, it is plausible, that zwitter-ionic propagating species favor the deprotonation of secondary amides over primary amides and thus more branching is occurring.

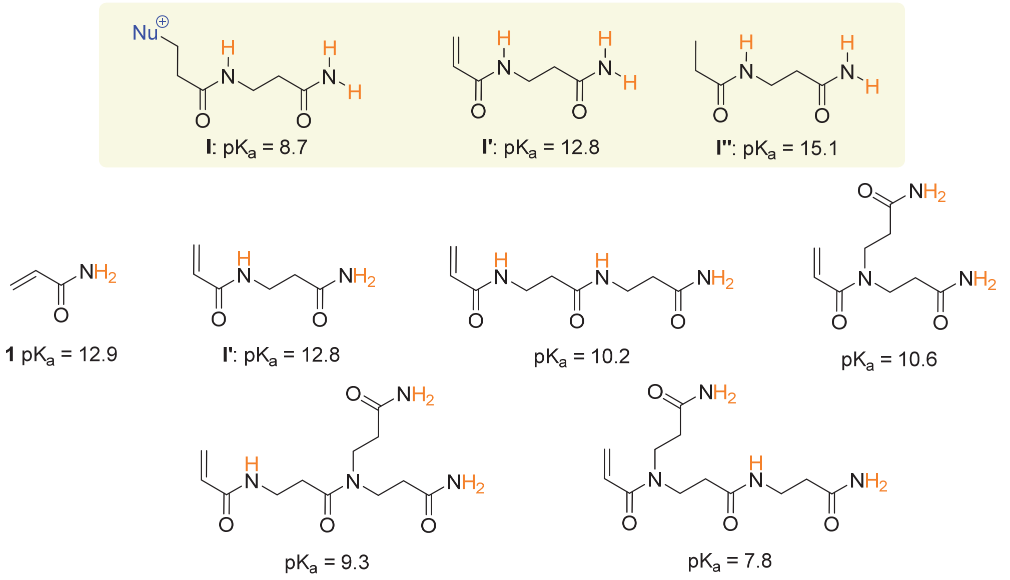


Figure 3. above, boxed in: pK_a-values of different potential dimers. below: pK_a-values of different mono- di-, tri- and tetramers of acrylamide. pK_a values calculated using the pK_a prediction platform (neural network result for solvent H_2O) available at pka.luo-group.com;[19] Nu = NMe_3.

A further effect of having the nucleophile attached to the growing chain is the higher acidity of such cationic species compared to neutral congeners. The boxed in section of Fig. 3 shows calculated pK_a values[19] of differently substituted dimers of type **I**. The pK_a values significantly increase within the series **I** < **I'** < **I''**. Therefore, it appears plausible that nucleophile bearing chains are preferably deprotonated. Furthermore, calculations suggest that pK_a values decrease with increasing number of repeat units (Fig. 3, below). Such a trend has been experimentally observed during studying the (basic) pK_a values of different series of well-defined peptides. Capillary zone electrophoresis of e.g. oligoglycines revealed a drop of their pK_a from 9.9 (monomer) to 8.2 (dimer) reaching eventually a plateau of about 7.9 (pentamer and higher oligomers).[28] Accordingly, the second question raised above can be answered. Because of the difference in acidity of the amides protons in monomers and in higher oligomers anions preferably exist within chains of higher molecular weight. Thus, higher oligomers grow further upon reacting with monomers (or di- and trimers). In this way, the chain-growth behavior of this polymerization, i.e. the formation of higher molecular weight polymers upon decreasing the nucleophile amount, can be rationalized.

The thermal stability of PA 3 obtained with 0.5 mol% DBU was determined by thermogravimetry and 2 mass% loss was found at 244 °C (Fig. S23). The main decomposition shows an inclination point at 360 °C, a temperature that is very similar to mostly linear PA 3.[11] The polymer is characterized by a glass transition temperature (T_g) of about 67 °C as determined by differential scanning calorimetry with a heating rate of 20 °C/min (Fig. 4). No melting point could be observed within the investigated temperature range. As expected, branching decreases the T_g as NaO^{t}Bu-initiated, almost linear PA 3 features a T_g of about 85 °C.[11] As mentioned, the optical appearance of the branched PA 3 at room temperature is transparent, colorless and clear, suggesting a fully amorphous glassy character.

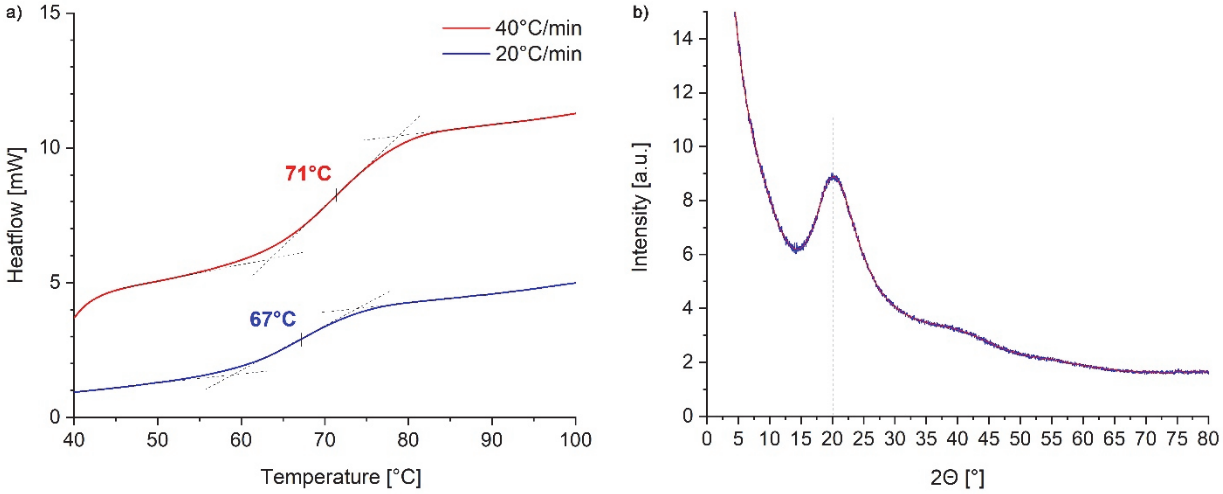


Figure 4. a) DSC of PA 3 prepared with 1 mol% DBU; red: 2nd heating run with a heating rate of 40 °C/min; blue 3rd heating run with 20 °C/min. b) Powder X-ray diffractogram (Cu-Kα) of PA 3 prepared with 1 mol% DBU.

To provide further insight, powder X-ray diffractometry was conducted and the obtained diffraction pattern consisted of series of three broad halos. No indication for any sign of crystallinity could be retrieved. The most intense feature peaked at a diffraction angle of about 20° and was accompanied with secondary features with higher diffraction angles (42° and 55°, Fig. 4).

Conclusions

Using nucleophiles in the initiation of the *aza*-Michael polymerization of acrylamide allows for the preparation PA 3 featuring a branching point at approx. every second repeat unit. The reaction is carried out in the melt of acrylamide and no solvents are involved in the preparation. Thus, a very simple and green route towards branched PA 3 became available. DBU has been identified as particularly suited initiator since only 0.5 mol% are sufficient for providing almost complete double bond conversion producing a PA 3 characterized by a number average molecular mass of about 23400 g/mol. The reaction exhibits a chain-growth character, which allows adjusting the molecular weight by variation of the nucleophile amount. The PA 3 prepared here is fully amorphous and exhibits a low T_g of 67 °C and good solubility in water as well as in dimethyl sulfoxide.

Experimental Section

Chemicals.

Acrylamide (**1**, 2-propenamide, 98%) was purchased from TCI, ^{15}N-ammonium chloride was purchased from Eurisotop, acryloyl chloride was purchased from ABCR, 1,4-diazabicyclo[2.2.2]octane (DABCO), triethylamine (NEt_3), 4-dimetylaminopyridine (DMAP), 1,8-diazabicyclo[5.4.0]undec-7-en (DBU), triphenylphosphine (PPh_3) and sodium *tert*-butoxide (NaO^{t}Bu, 97%) were purchased from Sigma-Aldrich. All chemicals were used as received except acryloyl chloride was distilled before use.

Instrumentation.

^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker Avance 300 MHz spectrometer at 25 °C (^{1}H: 300.36 MHz; ^{13}C: 75.53 MHz) or an Unity Inova 500 MHz High Resolution FT NMR from Varian equipped with an ^{1}H{^{15}N-^{31}P} 5 mm PFG indirect detection probe or an ^{1}H-^{19}F / ^{15}N-^{31}P 5 mm switchable probe (^{1}H: 500.13 MHz; ^{13}C: 125.76 MHz; ^{15}N: 50.70), which was particularly used for recording the ^{15}N-NMR spectra (referenced to ^{15}N-nitromethane). Chemical shifts δ are given in ppm relative to residual protons and carbon signals of the deuterated solvent. In case of spectra recorded in D_2O, 2,2,3,3-D_4-3-(trimethylsilyl)propionic acid, sodium salt was used as reference. Deuterated solvents and standards were obtained from Cambridge Isotope Laboratories Inc.

Matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) measurements were performed on a Bruker UltrafleXtreme MALDI-TOF mass spectrometer (Bruker Daltonik, Germany). Samples were dissolved in Milli-Q water (10 mg mL^{-1}), and mixed with a solution of 2,5-dihydroxybenzoic acid in Milli-Q water (saturated solution) as a matrix and sodium chloride in Milli-Q water (10 mg mL^{-1}) as a cationizer in a volume ratio of 1:10:3. A 1 µL of thus-prepared solution was spotted on the target plate (dried-droplet method). The reflective positive ion mode was used to acquire the samples' mass spectra. Calibration was performed externally with a mixture of PMMA standards (MALDI validation set PMMA, Fluka Analytical), covering the measured molecular weight range, and using the nearest-neighbor position method.

Size-exclusion chromatography coupled to a multi-angle light-scattering photometer (SEC-MALS) measurements were performed using an Agilent Technologies pump series 1200 coupled to a Dawn Heleos-II multi-angle light-scattering photometer with a GaAs linearly polarized laser (λ_0 = 663 nm) and to an Optilab T-rEX interferometric refractometer (RI), operating at the same wavelength as the photometer (both instruments are from Wyatt Technology Corp., USA). The separations were carried out at 50 °C using PolarGel-M column (Agilent, USA) with a pre-column in 0.1 M solution of LiBr in dimethyl sulfoxide (DMSO) at a flow rate of 0.7 mL min^{-1}. The masses of the samples injected onto the column were typically 5.0×10^{-3} g, whereas the solution concentration was 5.0×10^{-2} g mL^{-1}. Data acquisition and evaluation was performed with Astra 7.3.1 (Wyatt Technology Corp., USA).

Thermogravimetric analysis (TGA) was performed with a Netzsch Simultaneous Thermal Analyzer STA 449C (crucibles: aluminium from Netzsch) under nitrogen flow. The heating rate was 10 °C/min until a final temperature of 550 °C was achieved. A helium flow of 50 $mL\cdot min^{-1}$ in combination with a protective flow of 10 $mL\cdot min^{-1}$ was used.

Differential scanning calorimetry (DSC) measurements were carried out with a Perkin Elmer DSC 8500 using aluminum sealed pans. Heating and cooling rates of 20 °C/min and subsequently 40 °C/min were used to cycle the sample between 200 °C and – 20 °C, starting at 23 °C. The glass transition temperature was determined from the second heating run (40 °C/min) and third heating run (20 °C/min).

For powder X-ray diffractometric investigations a Rigaku MiniFlex diffractometer operating with Cu K_α radiation with a wavelength of 0.15418 nm.

Experimental Procedures.

General procedures for the synthesis of PA 3.

Acrylamide (**1**, 1.00 g, 14.07 mmol) was placed in a Schlenk-tube, a magnetic stirrer bar was added and the reaction vessel was heated to 83 °C using a temperature controlled oil-bath. Presumably, due to short overheating, **1** melted (melting point: 85.5 °C, onset of melting at approx. 80 °C as determined by DSC, Fig. S1) and stayed liquid although the oil bath temperature equilibrated at 83 °C. Then the according amount of nucleophile or base was added. After 24 h the reaction mixture was removed from the oil bath and allowed to cool to room temperature whereupon a transparent colorless monolith was obtained. No purification of the product was undertaken.

The reaction of **1** in the Monowave 50 reactor (from Anton Paar GmbH) was carried out with **1** (100 mg; 1.41 mmol) and DMAP (8.6 mg; 0.07 mmol). Both components were added into a reaction vessel and held at different temperatures for different times. Reaction conditions were: 200 °C for 0.5 h (double bond conversion: 97 %); 183 °C for 1 h (double bond conversion: 96%); 160 °C for 2 h (double bond conversion: 97 %); 140 °C for 3 h (double bond conversion: 97 %); 120 °C for 6 h (double bond conversion: 96%); 100 °C for 12 h (double bond conversion: 95.5%) and 83 °C for 24 h (double bond conversion: 91 %). No purification of the product was undertaken.

Preparation of ^{15}N-acrylamide.

$^{15}NH_4Cl$ (1.00 g, 18.35 mmol) and K_2CO_3 (2.58 g, 18.35 mmol) in diethyl ether (50 mL) were placed in a two-necked round bottom flask equipped with a dropping funnel, a reflux condenser and a magnetic stirrer bar. A solution of acryloyl chloride (742 µL; 9.18 mmol) in diethyl ether (20 mL) was slowly added through the dropping funnel. After complete addition of acryloyl chloride, the reaction was stirred for 24 h at room temperature. The salt residue was filtered off and washed with diethyl ether (2 x 10 mL). After removal of the solvent under reduced pressure, a white solid was obtained. Yield: 213 mg (33 %). Characterization is in agreement with literature.[29] The resulting ^{15}N-acrylamide (200 mg, 2.78 mmol) was then polymerized with 2 mol% DBU (8.5 mg, 0.06 mmol) as described above.

Supporting Information. The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/xxx. DSC of acrylamide, NMR spectra, MALDI-TOF MS spectra, calculations of the average degree of branching according to Fréchet or Frey, SEC-MALS results, thermogravimetric results, supplementary mechanistic scheme and pK_a values calculated for more compounds (PDF).

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Author Contributions. The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

ACKNOWLEDGMENT

Funding by the Christian Doppler Research Association (Austrian Federal Ministry for Digital and Economic Affairs and the National Foundation for Research, Technology and Development) is gratefully acknowledged.

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