

Synthesis of new Biginelli polycondensates: renewable materials with tunable high glass transition temperatures

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Abstract

The Biginelli reaction was applied as a simple one-pot multicomponent polycondensation approach to efficiently synthesize a set of 15 new and fully renewable poly(3,4-dihydropyrimidin-2(1H)-one)s. One of six bis-acetoacetates or three bis-acetoacetamides, terephthalic aldehyde and (methyl)-urea were used as renewable starting materials in various combinations, hence significantly expanding the known set of monomers as well as polymer structures. The bis-acetoacetates and bis-acetoacetamides with different spacer lengths were synthesized in yields of up to 99% in a one-step process. Thermal analysis of the obtained set of polymers revealed high glass transition temperatures (T_g) ranging from 160 to 308 °C. The T_g was tunable in small steps of 10 °C by simple variation of bis-acetoacetate or bis-acetoacetamide monomers as well as the choice of (methyl)-urea. The poly(3,4-dihydropyrimidin-2(1H)-one)s showed good thermal stability with $T_{d5\%}$ values well above the respective high T_g values.

Supporting information may be found in the online version of this article.

Keywords: multicomponent reaction; Biginelli reaction; glass transition temperature; renewable resources; polycondensation

INTRODUCTION

Multicomponent reactions (MCRs) are defined as convergent one-pot reactions with high atom economy, in which three or more starting materials efficiently form complex product structures that contain structural elements of each starting material.^{1,2} One-pot procedures allow the reduction of workup steps, material use and energy consumption. Thus, one-pot MCRs allow shorter overall reaction times, fewer purification steps and generally lead to high overall yields providing a tool for more sustainable chemical processes.^{1,3,4} In addition, MCRs are a valuable tool for the field of combinatorial chemistry due to their modular character, enabling the quick synthesis of large compound libraries.^{5,6} Prominent examples are the Strecker amino acid synthesis (1850),⁷ the Hantzsch dihydropyrimidin synthesis (1881),⁸ the Biginelli dihydropyrimidinone synthesis (1891),⁹ the Mannich aminomethylation (1912),¹⁰ as well as the isocyanide based Passerini α -acyloxy amide synthesis (1921)¹¹ and the Ugi bis-amide synthesis (1959).^{2,11}

Besides being a valuable tool for target-oriented synthesis¹² and diversity oriented synthesis,¹³ MCRs receive increasing interest from polymer and material scientists.^{14–16} The properties of a polymer mainly depend on the chemical structure, the sequence of the repeating units and the topology. All three can be controlled via MCRs. More precisely, MCRs allow the synthesis of interesting new monomers for known polymerization techniques, for instance the ring-opening metathesis polymerization of norbornene monomers synthesized via the Ugi four-component

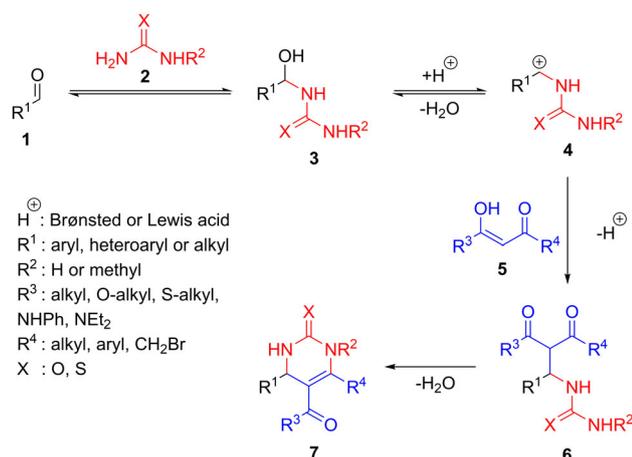
reaction,¹⁷ and enable the direct polymerization of multifunctional components. This was shown for a Passerini polyaddition of a dicarboxylic acid, a dialdehyde and various isocyanides.¹⁸ Moreover, it is possible to readily synthesize new polymers via post-polymerization modification techniques, as shown in the modification of a substituted polymethacrylate copolymer via the Biginelli reaction.¹⁹

The Biginelli-3-component reaction (Biginelli-3CR) was first described in 1891 by Pietro Biginelli, who observed the formation of a precipitate during the reaction of benzaldehyde, ethyl acetoacetate and urea in ethanol with catalytic amounts of hydrochloric acid.⁹ Later, Biginelli identified the precipitate as 3,4-dihydropyrimidin-2(1H)-one (DHPM).²⁰ The Biginelli-3CR and the resulting DHPMs were investigated due to their pharmaceutical activity, e.g. for the treatment of cardiovascular diseases,

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Scheme 1. Proposed mechanism of the Biginelli reaction:²⁴ hemiaminal **3** formation via addition reaction of aldehyde **1** and urea compound **2**, followed by acidic dehydration and interception of the iminium species **4** by 1,3-dicarbonyl **5**. Subsequent cyclization of **6** yields the DHPM **7**.

benign prostatic hyperplasia or as cancer treatment,²¹ prior to becoming an interesting tool for polymer chemists.^{22,23} Different mechanisms for the Biginelli-3CR have been discussed in the literature.^{24–27} The currently accepted mechanism for the formation of DHPMs in solution under Brønsted acid catalysis was published by Kappe in 1997.²⁴ Accordingly, the reaction starts with a nucleophilic addition of urea compound **2** to aldehyde **1** forming the hemiaminal **3**.²⁴ Subsequently, acid promoted dehydration leads to a highly reactive *N*-acyliminium ion **4**, which reacts with the 1,3-dicarbonyl **5**.²⁴ The resulting intermediate **6** undergoes cyclocondensation yielding the DHPM **7** (Scheme 1).²⁴ The rate determining step is considered to be the first addition of **1** and **2**.²⁴ The application of bifunctional molecules like terephthalic acid and bis-acetoacetates leads to the formation of Biginelli polycondensates.

Applying the post-polymerization modification approach, the Biginelli-3CR was used to modify starch.²⁸ It was additionally used as a tool to build polymer libraries from a polymer precursor with acetoacetate moieties in its backbone,²⁹ besides the above mentioned synthesis of a water soluble adhesive.¹⁹ The first Biginelli polycondensates were synthesized by Tao and colleagues using the direct polymerization approach and were applied as adhesives.³⁰ Later, the same group reported on the synthesis of copolycondensates by a combination of the Biginelli-3CR and the Hantzsch dihydropyridine synthesis³¹ and showed three possible post-polymerization modifications of poly(dihydropyrimidine thiones).³² In addition, they built a library of Biginelli polycondensates to predict the glass transition temperature (T_g) of polycondensates within the mapped spectrum of compounds.³³ In 2016, Meier *et al.* reported on the synthesis of renewable Biginelli polycondensates with high and tunable T_g s by a variation of the applied dialdehydes and bis-acetoacetates.³⁴

Herein, we report on the synthesis and comparison of novel renewable poly(DHPM)s (Scheme 2). We introduce (i) methyl-urea and (ii) three bis-acetoacetates as well as (iii) three bis-acetoacetamides to the set of starting materials described in the literature so far. This set includes (thio-)urea, terephthalic aldehyde, divanillin and bis-acetoacetates^{33,34} besides several AB-monomers^{30,31} containing aldehyde and acetoacetate moiety in different combinations. The resulting polymers are fully

characterized and show very high, tunable T_g s of up to 308 °C. Importantly, all starting materials can be derived from renewable resources.^{34,35}

MATERIALS AND METHODS

Materials

1,4-Butanediol (99%), 1,10-decanediamine (97%), 1,10-decanediol (98%), 1,2-ethylenediamine (99%), 1,6-hexanediamine ($\geq 99.0\%$), methyl-urea (97%), potassium trifluoroacetate (98%), 1,3-propanediol (98%), terephthalic aldehyde (99%) and 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (95%, diketene acetone adduct) were supplied by Sigma (Munich, Germany). Dimethyl sulfoxide (99.7%), 1,6-hexanediol (97%), *p*-toluenesulfonic acid (99%) and *tert*-butylacetoacetate (97%) were supplied by Acros Organics (Geel, Belgium). Ethylene glycol ($\geq 99.5\%$) was bought from Honeywell Riedel-de Haën (Charlotte, North Carolina, USA). 1,1,1,3,3,3-Hexafluoroisopropanol (HFIP) was purchased from Fluorochem (Haddington, United Kingdom). Urea and the solvents cyclohexane, ethyl acetate and methanol were used in technical grade without further purification.

General methods and instrumentation

Thin layer chromatography (TLC)

Fluorescent silica coated aluminium plates were used for TLC. The plates were developed using either a UV lamp to quench fluorescence at 254 nm or to excite fluorescence of the compounds at 365 nm, or Seebach stain (phosphomolybdic acid, cerium(IV) sulfate, sulfuric acid, water) to visualize UV-inactive compounds. The R_f values and used solvent mixtures are given in the respective synthesis procedure of each compound.

Flash column chromatography

Flash column chromatography was performed using a method similar to the method introduced by Still *et al.*³⁶ The glass column with built in fritted glass filter was filled with a slurry of eluent (the eluent is given in the respective synthesis procedure of each compound) and stationary phase (silica, Aldrich, technical grade, 60 Å pore size, 230–400 mesh size, 40–63 μm particle size). The crude substance was applied in a liquid state dissolved in a small amount of eluent. The pressure was applied with a manual pump.

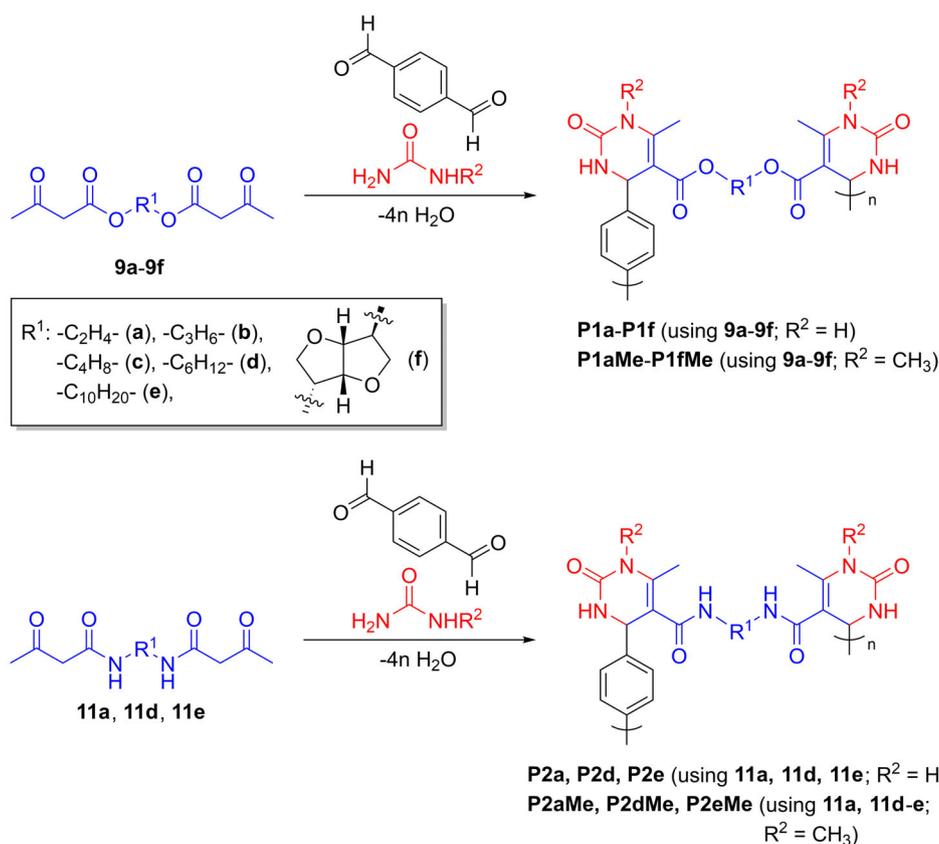
Nuclear magnetic resonance (NMR) spectroscopy

^1H and ^{13}C NMR spectra were recorded on a Bruker Avance NEO spectrometer at a frequency of 400.13 MHz and 100.62 MHz, respectively. For sample preparation, 10–15 mg of substance were dissolved in approximately 0.50 mL deuterated dimethyl sulfoxide (DMSO-d_6) (99.80 at% D) in an NMR tube with a diameter of 5 mm. The chemical shift (δ) was given in parts per million (ppm) relative to δ of tetramethylsilane ($\delta(\text{TMS}) = 0.00$ ppm).

The chemical shifts of DMSO-d_6 were used for referencing: ^1H NMR 2.50 ppm; ^{13}C NMR 39.52 ppm. Splitting patterns were denoted as follows: s (singlet), d (doublet), dd (doublet of doublets), t (triplet), q (quartet), p (pentet), m (multiplet) and br (broad). The respective coupling constants xJ were given in hertz (Hz).

Infrared (IR) spectroscopy

IR spectra were recorded on a Bruker Alpha FTIR spectrometer equipped with platinum ATR technology. The resulting transmittance spectra were averaged from 24 measurements. The energies of the IR bands were given in cm^{-1} .



Scheme 2. Preparation of poly(DHPM)s using **9a-9f** or **11a, 11d** and **11e** (blue), terephthalic aldehyde (black) and (methyl)-urea (red). The resulting polymers **P1a-P1f**, **P1aMe-P1fMe**, **P2a, P2d, P2e**, **P2aMe, P2dMe** and **P2eMe** show highly tunable T_g s from 160 to 308 °C.

High resolution mass spectrometry (HRMS)

High resolution mass spectra were recorded on a Finnigan MAT 95 spectrometer using electron ionization.

Vacuum oven

Polymer samples were dried in a ThermoScientific™ VacuTherm VT6025 S vacuum drying oven at 100 °C under vacuum prior to analysis.

Size exclusion chromatography (SEC)

SEC was performed on a Tosoh EcoSEC HLC-8320 SEC system. For sample preparation, 2 mg of sample were dissolved in 2 mL hexafluoroisopropanol with 0.1wt% potassium trifluoroacetate. The same solvent mixture was used as mobile phase. The solvent flow was 0.40 mL min⁻¹ at 35 °C. The analysis was performed on a three-column system: PSS PFG Micro precolumn (3.0 × 0.46 cm, 10 000 Å), PSS PFG Micro (25.0 × 0.46 cm, 1000 Å) and PSS PFG Micro (25.0 × 0.46 cm, 100 Å). The system was calibrated with linear poly(methyl methacrylate) standards (PSS, M_p 102–981 kDa).

Differential scanning calorimetry (DSC)

DSC experiments were performed on a DSC821e (Mettler Toledo) calorimeter. Samples were prepared by compressing 15–20 mg of sample in a 100 µL aluminium crucible. The measurements were performed under a nitrogen atmosphere with two heating cycles in the temperature range –50 to 300 °C (or –50 to 350 °C) with a cooling rate of 15 K min⁻¹ and a heating rate of 30 K min⁻¹.

For the calculation of the thermal transitions, the second heating cycle was used. The T_g s were determined using the inflection points of the respective second-order transitions.

Thermogravimetric analysis (TGA)

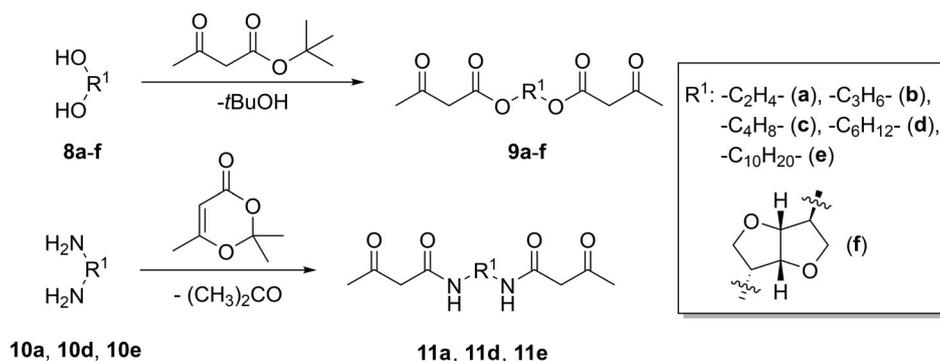
The TGA was performed on a Netzsch STA 490C with Al₂O₃ as the crucible material and reference sample. The samples of 10–20 mg were heated from room temperature to 500 °C with a temperature gradient of 5 K min⁻¹ under synthetic air flow. The temperature at which a weight loss of 5% is reached ($T_{d5\%}$) was determined via intersection of the TGA curve with a line at $y = 0.95 - a$, where a is the weight loss at 105 °C (to exclude the weight loss due to water evaporation).

Bis-acetoacetate and bis-acetoamide synthesis

Bis-acetoacetates

All bis-acetoacetates were synthesized using the following general procedure. The respective diol (1.00 eq) was mixed with *tert*-butylacetoacetate (*t*-BuAA) (5.00 eq) and stirred in a preheated oil bath at 150 °C for 7 h. Evolving *tert*-butyl alcohol (*t*-BuOH) was continuously removed via distillation. Afterwards, the crude product was purified by column chromatography using a gradual mixture of *c*-C₆H₁₂ and EtOAc. The formed *t*-BuOH as well as the excess of *t*-BuAA were recovered via distillation and column chromatography, respectively.

Detailed information on the synthesis, purification and analytical data of all bis-acetoacetates is available in the Supporting information.



Scheme 3. Bis-acetoacetate monomer synthesis: reaction of diols **8a–8f** with *tert*-butylacetoacetate in bulk yielding **9a–9f**; reaction of **10a**, **10d** and **10e** with 2,2,6-trimethyl-4H-1,3-dioxin-4-one in bulk yielding **11a**, **11d** and **11e**.

Bis-acetoacetamides

All bis-acetoacetamides were synthesized using the same general procedure. The respective diamine (1.00 eq) was added dropwise to preheated (130 °C) 2,2,6-trimethyl-4H-1,3-dioxin-4-one (2.10 eq) under vigorous stirring. Afterwards, the mixture was stirred at 130 °C for 5 h. Subsequently, the mixture was cooled to 100 °C and ethanol was directly added to the hot mixture in order to recrystallize the crude product. The resulting white/off-white crystals were filtered, washed with cold ethanol and dried under high vacuum ($<10^{-2}$ mbar).

Detailed information on the synthesis and analytical data of all bis-acetoacetamides is available in the Supporting information.

Polymer synthesis

General procedure for poly(DHPM)s

All poly(DHPM)s were synthesized according to the same general procedure. Nevertheless, the reaction times and the solvent/solvent mixture that was used for precipitation and washing (depending on the polymer structure (details are given for the respective polymer)) differed.

(Methyl)-urea (3.50 eq) and the respective bis-acetoacetate (or bis-acetoacetamide) (1.00 eq) were mixed in DMSO (1 mol L⁻¹ solution regarding 1.00 eq). Afterwards, terephthalic aldehyde (1.00 eq) and *p*-toluenesulfonic acid (0.10 eq) were added.

The mixture was immediately heated to 125 °C in a preheated oil bath and stirred for 22.5 h (30 min for **P2aMe**, **P2dMe** and **P2eMe** each and 1.5 h for **P2e**). The flask was left open to allow water to evaporate. Afterwards, the polymer solution was precipitated in 100 mL of the respective solvent/solvent mixture and stirred for 3 h. Subsequently, the precipitated polymer was filtered and washed with the same solvent/solvent mixture. The resulting material was dried in a vacuum drying oven overnight at 85 °C under reduced pressure resulting in the final product.

Detailed information on the synthesis, purification and analytical data of all polymers is available in the Supporting information.

Samples for kinetic investigation via SEC were prepared by precipitating 5 μ L of the reaction mixture in water. After decanting and drying in a vacuum oven the samples were dissolved in 2 mL HFIP with 0.1 wt% KCO₂(CF₃).

RESULTS AND DISCUSSION

Monomer synthesis

A known procedure³⁴ was optimized and simplified to synthesize the bis-acetoacetate monomers **9a–9f** with yields between 98%

and 99% by stirring the renewable diols **8a–8f** and *t*-BuAA at 150 °C for 7 h in bulk (Scheme 3). To further improve the sustainability of the monomer synthesis, up to 90% of *t*-BuOH (via distillation during the reaction) and 95% of excess *t*-BuAA (via column chromatography during product purification) were recovered. **9a–9f** were characterized by ¹H and ¹³C NMR spectroscopy, IR and HRMS. The respective ¹H NMR spectra showed the characteristic signals of the α -CH₂ protons at 3.2 ppm and the signals of the terminal γ -CH₃ protons of the β -ketoester moiety at 2.2 ppm. According to NMR spectroscopy, less than 3 mol% EtOAc remained in the purified monomers. Besides the aliphatic diols, isosorbide was chosen as a diol, since it is the best suitable and available example of a renewable diol that offers high *T*_gs in a variety of different polymers.³⁷

The bis-acetoacetamide monomers **11a**, **11d** and **11e** were synthesized with yields up to 62%, similarly to a procedure by Clemens and Hyatt,³⁸ by reacting a series of diamines **10a**, **10d** and **10e** with 2,2,6-trimethyl-4H-1,3-dioxin-4-one (Scheme 3, bottom). **11a**, **11d** and **11e** were characterized by ¹H and ¹³C NMR spectroscopy, IR and HRMS. The ¹H NMR spectra showed the characteristic signals of the α -CH₂ protons at 3.3 ppm and the signals of the terminal γ -CH₃ protons of the β -ketoamide moiety at 2.1 ppm. According to NMR spectroscopy, the pure monomers were obtained. All NMR data and assignments are provided in the Supporting information.

To address the renewable character of the poly(DHPM)s, the renewability of the applied starting materials is summarized in this section. The used diols can be obtained from sugars,^{39,40} while acetoacetates are accessible via Claisen condensation⁴¹ of ethyl acetate, which itself can be derived by cellulose hydrolysis.⁴⁰ Diamines can either be synthesized from diols or nitrogen containing biomass like chitin or proteins.³⁵ Terephthalic aldehyde can be biobased as well. Common sustainable synthesis routes towards terephthalic acid start from biobased hydroxymethyl furan or isobutanol, both leading to *p*-xylene.^{42,43} The latter can possibly be oxidized to terephthalic aldehyde.³⁴

Poly(DHPM)s

Poly(DHPM)s using bis-acetoacetates

First, the polymerization kinetics were investigated for **P1e**, **P1eMe**, **P1f** and **P1fMe** (see the Supporting information for details) to establish suitable polymerization conditions. Thus, samples for SEC were taken after certain time intervals monitoring molecular weights and dispersities \bar{D} . The polymerization was stopped by precipitation of aliquots of the reaction mixture into

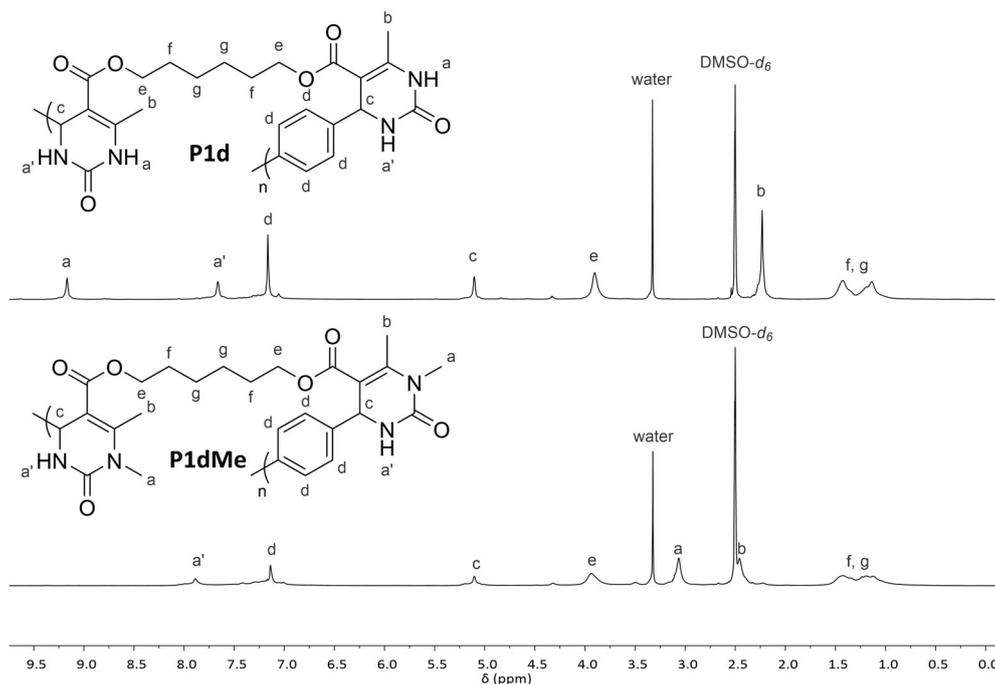


Figure 1. ^1H NMR spectra of **P1d** (top) and **P1dMe** (bottom) showing, as examples, the characteristic signals of poly(DHPM)s from bis-acetoacetates.

water to remove (methyl)-urea. The molecular weights and dispersities \bar{D} of **P1e** and **P1eMe** increased over time and reached an M_n of 4.9 kDa ($\bar{D} = 3.24$) and 8.7 kDa ($\bar{D} = 2.88$), respectively, when the reaction was stopped after 22.5 h. If **9f** was used as bis-acetoacetate, the M_n of **P1f** and **P1fMe** developed similarly, while the mass distributions were significantly broader after 22.5 h ($\bar{D} = 10.1$ and 13.1, respectively). Since sufficiently high molecular weights were obtained under these conditions, the same conditions were chosen for the polycondensations **P1a–P1f** and **P1aMe–P1fMe** obtaining similar molecular weights. Some of these molecular weights, and especially the obtained dispersities, are atypical for polycondensation reactions. This will be discussed in the following sections.

The poly(DHPM)s **P1a–P1f** or **P1aMe–P1fMe** were synthesized using stoichiometric amounts of bis-acetoacetates **9a–9f** and terephthalic aldehyde, as well as a 1.75-fold excess of (methyl)-urea and 10 mol% of *p*-toluenesulfonic acid as a catalyst in DMSO as solvent. After the reaction, the polymer was precipitated and subsequently dried in a vacuum oven yielding the final polymer in yields up to 86%. The polymers were fully characterized using ^1H NMR, SEC, DSC, IR and TGA. The ^1H NMR spectra of poly(DHPM)s **P1a–P1f** showed the characteristic signals (Fig. 1, top example shows the ^1H NMR spectrum of **P1d**) of the NHC=C protons at 9.2 ppm, the NHC=C at 7.7 ppm, the aromatic protons around 7.2 ppm, the NH-CH-C_{Ar} protons at 5.1 ppm and the O=CO-CH₂ protons at 3.9 ppm. The signal of the C=C-CH₃ protons was visible at 2.3 ppm. Signals for aliphatic protons were furthermore visible between 1.5 and 1.1 ppm for poly(DHPM)s with aliphatic spacers longer than C₂H₄. For **P1aMe–P1fMe** (Fig. 1, bottom example shows the ^1H NMR spectrum of **P1dMe**), the signal at 9.2 ppm was absent while a new signal for the H₃C-NC=C protons at 3.0 ppm was observed. The NHC=C proton was shifted by +0.2 to 7.9 ppm and the C=C-CH₃ protons were shifted by +0.2 to 2.5 ppm. The signals of the aldehyde end-groups are observed at 10.2 ppm and were used to calculate the M_n s of the poly(DHPM)s

(Table 1). The obtained results indicate a higher degree of polymerization for longer spacer units and methyl-urea, possibly due to better solubility of the respective polymers in the reaction solvent DMSO. **P1b**, **P1d** and **P1e** have already been reported³⁴ prior to this work. The ^1H NMR spectra and IR spectra correlate well, while molecular weights were higher by a factor of approximately 2 compared to this work. T_g s for **P1b** and **P1d** were not observed in these previous reports.³⁴

The molecular weight distributions of the poly(DHPM)s were investigated via SEC (Table 1; see also Figs S16 and S24 for chromatograms) using hexafluoroisopropanol with 0.1 wt% KCO₂(CF₃)₂ as eluent. Other eluents were not suitable due to the insolubility of the poly(DHPM)s in water, acetonitrile, methanol, ethanol, dimethylacetamide or tetrahydrofuran. **P1a–P1d** showed increasing $M_{n,SEC}$ values from 3.80 to 8.30 kDa ($M_{n,NMR}$ up to 12.2 kDa) with varying dispersities \bar{D} from 2.8 to 4.2. Two possible reasons for the increasing $M_{n,SEC}$ for longer spacers were considered in accordance with the NMR results. First, a larger size of the spacer unit resulted in a higher degree of polymerization and thus a larger hydrodynamic volume and consequently a higher $M_{n,SEC}$. Second, in a material with longer aliphatic spacer units, the frequency of hydrogen bonds throughout the material is lower, which possibly results in less intramolecular hydrogen bonding and thus a larger hydrodynamic volume. The $M_{n,SEC}$ of **P1e** did not follow this trend, perhaps due to the lower solubility of **P1e** in hexafluoroisopropanol with 0.1 wt% KCO₂(CF₃)₂. This possibly led to lower hydrodynamic volumes, overcompensating the above explanations for higher $M_{n,SEC}$ values. Low solubility and problems using SEC analysis, especially for higher degrees of polymerization, have already been reported³⁴ for poly(DHPM)s and are generally known for polymers with strong hydrogen bonding, such as polyamides or polyureas.

The $M_{n,NMR}$ values of **P1aMe–P1eMe** obtained by ^1H NMR end-group analysis show a similar trend with increasing $M_{n,NMR}$ for longer spacer units up to 36.7 kDa, while being considerably higher

Table 1. SEC and DSC data for polymers **P1a–P1f** and **P1aMe–P1fMe**

Sample	R ₁	M _{n,NMR} (g mol ⁻¹)	M _{n,SEC} (g mol ⁻¹)	M _{w,SEC} (g mol ⁻¹)	Đ	T _g (°C)
P1a	C ₂ H ₄	5500	3800	14 800	3.88	280
P1b	C ₃ H ₆	5700	4900	18 000	3.65	255
P1c	C ₄ H ₈	6100	5600	16 600	2.85	239
P1d	C ₆ H ₁₂	10 100	8300	34 700	4.20	220
P1e	C ₁₀ H ₂₀	12 200	6600	18 200	2.76	198
P1f	Isosorbide	30 700	6200	50 000	8.07	308
P1aMe	C ₂ H ₄	11 300	10 800	43 000	3.99	248
P1bMe	C ₃ H ₆	24 000	10 500	33 800	3.21	222
P1cMe	C ₄ H ₈	21 400	7600	19 700	2.58	211
P1dMe	C ₆ H ₁₂	31 800	9500	42 800	4.94	175
P1eMe	C ₁₀ H ₂₀	36 700	8700	24 900	2.88	159
P1fMe	Isosorbide	23 000	8400	73 100	8.71	266

compared to **P1a–P1e**. The $M_{n,SEC}$ values are decreasing with longer spacer units. In comparison with the poly(DHPM)s derived from urea, the $M_{n,SEC}$ values were higher with 6.70 to 10.8 kDa ($\bar{D} = 2.5\text{--}5.0$). Interestingly, the $M_{n,SEC}$ decreased with increasing $M_{n,NMR}$ (if the $M_{n,NMR}$ was above 11 kDa) for poly(DHPM)s from urea as well as methyl-urea.

The optimized synthesis of **P1f** and **P1fMe** led to polymers with a high $M_{n,NMR}$ of 30.7 and 23.0 kDa, respectively. The $M_{n,SEC}$ values were 6.2 and 8.4 kDa with broad dispersities ($\bar{D} = 8.07, 8.71$). Since the reaction mixtures of **P1f** and **P1fMe** were very viscous, the stirring was possibly not sufficient, thus leading to inhomogeneous polymerization mixtures throughout the reaction and hence to a broadened molecular weight distribution.

The results discussed are an important indication that the intramolecular hydrogen bonding in poly(DHPM)s, which is more pronounced for **P1a–P1e**, highly influences the reaction progress and leads to a compact structure in solution. Thus, small hydrodynamic volumes were observed by SEC. To conclude, a longer spacer or the use of methyl-urea seemed to accelerate the polymerization, while the hydrodynamic volume was dependent on the molecular weight rather than the molecular structure. Summarizing the molecular weight analysis, it is obvious that the obtained values must be considered with care, as an accurate analysis is difficult due to the mentioned solubility and aggregation issues. Nonetheless, the results clearly show that sufficiently high molecular weight polycondensates were obtained as confirmed by SEC and NMR.

The influence of the choice of urea/methyl-urea and bis-acetoacetate on the thermal properties of the poly(DHPM)s was investigated via DSC. Generally, the poly(DHPM)s showed T_g values between 160 and 308 °C (Table 1), as expected from the highly rigid and strongly hydrogen bonding repeating units. Comparing the T_g s, a clear trend was observed: the T_g s were lower for polymers with longer spacers. This seems reasonable considering the above assumptions that an increasing spacer length resulted in decreasing hydrogen bond frequency and thus increased flexibility of the polymer backbone. In addition, if the same bis-acetoacetate was used, the respective T_g was lower for polymers **P1aMe–P1eMe** compared to **P1a–P1e**. In line with the above considerations, **P1f** and **P1fMe** showed the highest T_g s of 308 and 266 °C, respectively, due to the rigid bicyclic structure of isosorbide. Considering all data (Table 1), it was possible to adjust the T_g of the poly(DHPM)s (**P1a–P1f** and **P1aMe–P1fMe**) in small steps (<10 °C) within a 150 °C range from 160 to 308 °C

by a simple variation of the combination of starting materials. The T_g s of other renewable polymers from various resources are usually below 150 °C.³⁷ Several other renewable polymers with a higher T_g are known. For example, polyamides with a T_g of 273 °C were obtained using monomers synthesized via [2 + 2]-cycloaddition of 4-aminocinnamic acid.⁴⁴ Applying isosorbide and its diastereomers isomannide and isoidide as monomers, different polyesters with a T_g between 180 and 196 °C^{45–48} and polycarbonates with a T_g up to 175 °C were obtained.^{49,50}

TGA revealed that the poly(DHPM)s from bis-acetoacetates have high thermal stability under synthetic air flow. The observed $T_{d5\%}$ values were between 264 and 314 °C (Table S11). The $T_{d5\%}$ of **P1a–P1e** and **P1aMe–P1fMe** surpassed the respective T_g s, indicating a possible thermal processing of these polymers. However, the $T_{d5\%}$ of **P1f** was lower (289 °C) than its T_g at 308 °C.

Poly(DHPM)s using bis-acetoacetamides

The investigation of the polymerization kinetics of **P2e** and **P2eMe** (see the Supporting information) revealed that an insoluble gel was formed if the reaction time was longer than approximately 2.5 h for **P2e** and 0.5 h for **P2eMe**. The gelation is indicated by a broadening of the molecular weight distribution (shoulder at high molecular weights) prior to gelation (see Figs S32 and S37). As a consequence, the synthesis of **P2e** was stopped after 1.5 h. The reaction time of **P2a** and **P2d** was kept at 22.5 h, since no gelation was observed. The polymerizations **P2aMe**, **P2dMe** and **P2eMe** were stopped after 0.5 h to avoid gelation. Except for the reaction time, the same procedure as for **P1a–P1f** and **P1aMe–P1fMe** was applied yielding poly(DHPM)s in yields of up to 67%.

The polymers were fully characterized using ¹H NMR, SEC, DSC, IR and TGA. **P2a**, **P2d** and **P1e** showed the characteristic signals (Fig. 2, top example shows the ¹H NMR spectrum of **P2d**) of the NHC=C protons at 8.5 ppm, the NHC-C at 7.6 ppm, the O=C (NH)-CH₂ at 7.5 ppm, the aromatic protons around 7.2 ppm, the NH-CH-C_{Ar} proton at 5.2 ppm and the O=C(NH)-CH₂ protons at 3.1 ppm. The signal of the C=C-CH₃ protons was observed at 2.0 ppm. Signals for aliphatic protons were furthermore visible between 1.5 and 0.9 ppm for poly(DHPM)s with aliphatic spacers longer than C₂H₄. For **P2aMe**, **P2dMe** and **P1eMe** (Fig. 2, bottom example shows the ¹H NMR spectrum of **P2dMe**), the signal at 8.5 ppm was absent, while a new signal for the H₃C-NC=C protons at 3.0 ppm was observed, overlapping with the broad O=C (NH)-CH₂ signal. The latter was confirmed via phase edited

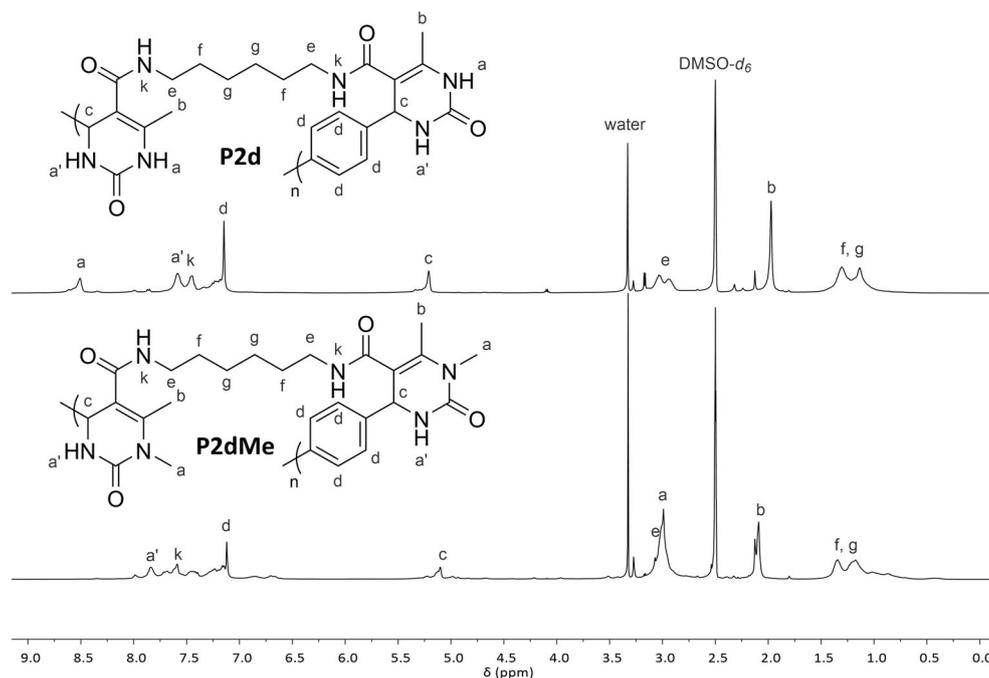


Figure 2. ^1H NMR spectra of **P12d** (top) and **P2dMe** (bottom) showing, as examples, the characteristic signals of poly(DHPM)s from bis-acetoacetamides.

Table 2. SEC and DSC data of polymers **P2a**, **P2d**, **P2e**, **P2aMe**, **P2dMe** and **P2eMe**

Sample	R_1	$M_{n,NMR}$ (g mol^{-1})	$M_{n,SEC}$ (g mol^{-1})	$M_{w,SEC}$ (g mol^{-1})	\bar{D}	T_g ($^{\circ}\text{C}$)
P2a	C_2H_4	9600	5000	23 400	4.71	— ^a
P2d	C_6H_{12}	5300	12 400	63 000	5.07	265
P2e	$\text{C}_{10}\text{H}_{20}$	5500	11 800	40 300	3.40	235
P2aMe	C_2H_4	2400	6000	12 400	2.06	— ^a
P2dMe	C_6H_{12}	3900	5300	13 000	2.47	— ^a
P2eMe	$\text{C}_{10}\text{H}_{20}$	3800	15 200	71 100	4.71	194

^a Not observed.

heteronuclear single quantum coherence spectroscopy (Fig. S42). The $\text{NH}-\text{C}$ proton remained at 7.6 ppm, the $\text{O}=\text{C}(\text{NH})-\text{CH}_2$ was shifted by +0.3 to 7.8 ppm, the $\text{NH}-\text{CH}-\text{C}_{Ar}$ proton was shifted -0.1 to 5.1 ppm, and the $\text{C}=\text{C}-\text{CH}_3$ protons were shifted by +0.2 to 2.2 ppm.

The obtained molecular weights ($M_{n,SEC}$) of the resulting polymers were 5.00 kDa (**P2a**), 12.4 kDa (**P2d**) and 11.8 kDa (**P2e**), 6.00 kDa (**P2aMe**), 5.30 kDa (**P2dMe**) and 15.2 kDa (**P2eMe**). \bar{D} ranged from 2.06 to 5.07 (Table 2). With respect to their $M_{n,NMR}$, the poly(DHPM)s from bis-acetoacetamides seemed to show larger hydrodynamic radii compared to the poly(DHPM)s from bis-acetoacetates.

A T_g (Table 2) was observed for **P2d** (265 $^{\circ}\text{C}$), **P2e** (235 $^{\circ}\text{C}$) and **P2eMe** (194 $^{\circ}\text{C}$). Compared to **P1d** (220 $^{\circ}\text{C}$), **P2e** (198 $^{\circ}\text{C}$) and **P2eMe** (159 $^{\circ}\text{C}$), respectively, the T_g s were expectedly higher (35–45 $^{\circ}\text{C}$ higher compared to poly(DHPM)s from bis-acetoacetates) for the polymers that contained an amide moiety due to additional hydrogen bonding. No thermal transition was observed for **P2a**, **P2aMe** and **P2dMe**, although different heating/cooling rates for DSC investigations (range of 5–35 K min^{-1}

and 5–20 K min^{-1} , respectively) were considered. For **P2a** it is possible that the T_g is above the $T_{d5\%}$ and is therefore not observable. Consequently, the T_g s for bis-acetoacetamide derived poly(DHPM)s can possibly be tuned in a similar manner compared to bis-acetoacetate derived poly(DHPM)s. A TGA showed that the poly(DHPM)s from bis-acetoacetamides have high thermal stability under synthetic air flow. The observed $T_{d5\%}$ values were 278–314 $^{\circ}\text{C}$ (Table S11) and thus in a similar range to the poly(DHPM)s from bis-acetoacetates.

CONCLUSION

Herein, we synthesized a set of 15 new poly(DHPM)s via Biginelli polycondensation introducing methyl-urea and several bis-acetoacetate and bis-acetoacetamide monomers as new building blocks. In addition, three literature known poly(DHPM)s, which fit in this series of investigated polymers, were prepared. The T_g of two of them was analysed for the first time. The monomers can be derived from renewable resources in yields from 43% to 99%. T_g s of the resulting polymers were tunable in small steps of

approximately 10 °C from 160 to 308 °C by exploitation of the established structure–property relations, rendering poly(DHPM)s more sustainable alternatives for high T_g thermoplastics. In addition, the high thermal stability of the poly(DHPM)s potentially allows for thermal processing techniques.

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SUPPORTING INFORMATION

Supporting information may be found in the online version of this article.

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