### Structurally Diverse Polyamides Obtained from Monomers Derived via the Ugi Multicomponent Reaction

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Abstract: The combination of the Ugi four-component reaction (Ugi-4CR) with acyclic diene metathesis (ADMET) or thiol-ene polymerization led to the formation of poly-1-(alkylcarbamoyl) carboxamides, a new class of substituted polyamides with amide moieties in the polymer backbone, as well as its side chains. 10-Undecenoic acid, obtained by pyrolysis of ricinoleic acid, the main fatty acid of castor oil, was used as the key renewable building block. The use of different primary amines, as well as isonitriles (isocyanides) for the described Ugi reactions provided monomers with high structural diversity. Furthermore, the possibility of versatile post-modification of

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functional groups in the side chains of the corresponding polymers should be of considerable interest in materials science. The obtained monomers were polymerized by ADMET, as well as thiol–ene, chemistry and all polymers were fully characterized. Finally, *ortho*nitrobenzylamide-containing polyamides obtained by this route were shown to be photoresponsive and exhibited a dramatic change of their properties upon irradiation with light.

### Introduction

Isocyanide-based multicomponent reactions (IMCRs) have been known since Passerini developed the first three-component reaction (Passerini-3CR) between a carboxylic acid, an aldehyde, and an isocyanide (isonitrile) in 1921.<sup>[1]</sup> The best-known and most famous IMCR is the Ugi four-component reaction (Ugi-4CR). In 1959, Ugi et al. discovered that an aldehyde (ketone) and a primary amine react with a carboxylic acid and an isonitrile to form substituted a-amino acylamides.<sup>[2]</sup> In this reaction two substituted amide groups are formed under release of one equivalent of water. Thus, the Ugi-4CR is an atom-economic and environmentally friendly reaction. It was also shown that water can be used as the solvent.<sup>[3]</sup> This reaction is typically performed by stirring the components for approximately 1 day in small quantities of a protic solvent (e.g., methanol or trifluoroethanol). The desired products are usually obtained in moderate to

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Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201103341. It includes full compound characterization (GPC, NMR, and DSC), experimental details, synthesis procedures, and additional results. high yields ranging from 40 to 90%. Due to the high tolerance for other functional groups, a broad spectrum of components can be applied and thus the Ugi-4CR and related multicomponent reactions, as well as a range of post-modifications, are very valuable approaches in combinatorial and medicinal chemistry for the development of new pharmaceuticals.<sup>[4]</sup> Moreover, the Ugi-4CR has become more and more attractive in key steps of natural product syntheses.<sup>[5]</sup> Wessjohann et al. have shown that the Ugi reaction is a suitable approach in the construction of highly diverse and large macrocyclic molecules.<sup>[6]</sup> The application of the Ugi-4CR in polymer chemistry is to date very limited. Only in 2003 did Wright et al. describe ring-opening polymerization (ROMP) with products derived from the Ugi-4CR with norbornenyl starting materials.<sup>[7]</sup>

To introduce the Ugi-4CR in the synthesis of highly diverse substituted polyamides,  $\alpha, \omega$ -diene monomers were synthesized by the Ugi reaction and then polymerized by applying the acyclic diene metathesis (ADMET) polymerization, as well as thiol–ene addition polymerization. To our knowledge, the combination of the Ugi-4CR and step-growth polymerization has not yet been reported. Recently, we were able to successfully demonstrate the ADMET polymerization of 1-(alkylcarbamoyl)alkyl alkanoates ( $\alpha$ -carbamoyl-substituted ester derivatives), derived through the Passerini-3CR with carboxylic acids and aldehydes containing terminal double bonds.<sup>[8]</sup>

A very useful source of the required olefin compounds are the pyrolysis products of castor oil, which finds a large number of applications for material syntheses in industry.<sup>[9a]</sup> With contents up to 97%, ricinoleic acid  $\mathbf{1}$  ((9*Z*,12*R*)-12-hydroxyoctadec-9-enoic acid) is the major fatty acid of castor

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oil triglycerides.<sup>[9b]</sup> The hydroxyl group of **1** makes this fatty acid attractive for chemical modifications, such as esterification, etherification, and synthesis of polyurethanes and polycarbonates from renewable sources. Moreover, the carboxylic group and the double bond are functionalities to modify **1** for favorable material properties.<sup>[9a]</sup> At temperatures above 350°C, **1** fragments to 10-undecenoic acid **2** and heptanal **3** (Scheme 1).<sup>[9c]</sup> Compound **2** is valuable in the chemi-



Scheme 1. Products of thermal fragmentation of ricinoleic acid 1, followed by Ugi-4CR and ADMET polymerization.

cal industry and has been used for a long time in the synthesis of the renewable polyamide-11.<sup>[9d]</sup> Recently, olefin metathesis has been shown to be a very useful approach to find new ways to polymers starting from **2**. For instance, olefin metathesis strategies such as self-metathesis and cross-metathesis of methyl 10-undecenoate with functionalized olefins, for example, acrylates, allylic alcohols, and acrylonitrile, led to compounds that are valuable starting materials for step-growth polymerization reactions to obtain polyesters and polyamides.<sup>[10a,b]</sup> Moreover, the ADMET polymerization is an excellent tool for the polymerization of  $\alpha, \omega$ -diene monomers. Due to the development of modern ruthenium-based metathesis catalysts, which tolerate numerous functional

groups, diverse  $\alpha, \omega$ -dienes were successfully applied in the ADMET polymerization.<sup>[10c]</sup> In 2001, Warwel et al. described renewable high-molecular-weight polyesters that were prepared by ADMET.<sup>[10d,e]</sup> Moreover, **2** was also shown to be a very useful compound for the preparation of monomers for ADMET polymerization.<sup>[10f]</sup> In addition, the 10-undecenyl ester of **2** was employed successfully in the synthesis of castor-oil-derived polymers through ADMET.<sup>[10-s-i]</sup> Recently, several reaction conditions, such as time, temperature, and screening of several ruthenium catalysts, as well as catalyst amounts, were optimized, thereby showing that 1,4-benzoquinone as additive to ADMET polymerizations can suppress undesired olefin-isomerization side reactions dramatically.<sup>[11]</sup>

Finally, the ADMET strategy was employed in the synthesis of poly- $\alpha$ , $\beta$ -unsaturated aldehydes starting from the aldol condensation product of 10-undecenal 4.<sup>[12]</sup> The results showed that several ruthenium-based metathesis catalysts tolerate the  $\alpha,\beta$ -unsaturated double bond during the ADMET process and no side products were formed. To expand the applications of 2, we investigated the behavior of 2 and its reduced product 10-undecenal 4 in IMCRs. Compound 4 is commercially available in technical quality at relatively fair prices and can be obtained from 2 or 10-undecenol in yields of up to 60% and higher.<sup>[13]</sup> An improvement in the synthesis of 4 for possible large-scale applications is, however, still required. Our aim was to introduce 2 and **4** in the Ugi-4CR with different isonitriles and primary amines, especially amino acid derivatives, to synthesize a library of  $\alpha, \omega$ -diene derivatives of Ugi products. The behavior of these products in the ADMET polymerization, as well as thiol-ene polymerization, another useful tool to polymerize  $\alpha,\omega$ -diene monomers, will be investigated. Recently, we described the thiol-ene polymerization of monomers derived from renewable sources.<sup>[14]</sup> Finally, all obtained polymers were characterized by NMR spectroscopy, gel permeation chromatography (GPC), and differential scanning calorimetry (DSC).

#### **Results and Discussion**

To create a small library of Ugi-4CR products derived from 10-undecenoic acid **2** and 10-undecenal **4**, different primary amines **5a–5k** and isonitriles **6a–6e** were used. First, Ugi-4CRs were performed by using benzylamine **5a** and its *para*-methoxy-substituted derivative **5b** in combination with commercially available cyclohexyl isonitrile **6a** and *tert*butyl isonitrile **6b** (Scheme 2, Table 1). After stirring for about 1 day at room temperature in small amounts of methanol, followed by purification by column chromatography, the Ugi-4CR products with  $\alpha,\omega$ -diene moieties **7a** and **7b** were obtained as light brown oils in rather good yields of 63 and 69%, respectively. Ugi-4CR product **7c** was obtained in a lower yield of 47% from *ortho*-nitrobenzylamine **5c** and methyl 4-isocyanobutyrate **6c** as an ester-functionalized isonitrile. Compound **6c** can be synthesized in a three-step pro-

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Scheme 2. Ugi-4CR with 10-undecenoic acid 2, 10-undecenal 4, primary amines 5a-5k, and isonitriles 6a-6e.

Table 1. Products 7a-7q of Ugi-4CRs derived from 2 and 4.[a]

Product	$\mathbb{R}^1$	<b>R</b> <sup>2</sup>	Yield [%]
7a	-Bn ( <b>5a</b> )	- <i>c</i> Hx (6a)	63
7b	- <i>p</i> -MeO-Bn (5b)	- <i>t</i> Bu (6b)	69
7c	-o-NO <sub>2</sub> -Bn (5c)	-(CH <sub>2</sub> ) <sub>3</sub> CO <sub>2</sub> Me ( <b>6</b> c)	47
7 d	-o-NO <sub>2</sub> -Bn (5c)	- <i>o</i> -NO <sub>2</sub> -Bn ( <b>6e</b> )	57
7e	-Gly-OMe (5d)	-cHx (6a)	55
7 f	-Gly-OMe (5d)	- <i>t</i> Bu (6b)	46
7g	-Ala-OMe (5e)	-cHx (6a)	61
7 ĥ	-D-Ala-OMe (5f)	-cHx (6a)	68
7i	-Val-OMe (5g)	-cHx (6a)	69
7j	-Phe-OMe (5h)	-cHx (6a)	56
7ĸ	-Ser-OMe (5i)	-cHx (6a)	51
71	-Gly-OMe (5d)	$-(CH_2)_3CO_2Me$ (6c)	53
7 m	-Gly-OtBu (5j)	$-(CH_2)_3CO_2Me$ (6c)	48
7 n	-(CH <sub>2</sub> ) <sub>2</sub> OH (5k)	- <i>c</i> Hx (6a)	54
70	-(CH <sub>2</sub> ) <sub>2</sub> OH (5k)	$-(CH_2)_3CO_2Me$ (6c)	29
<b>7 p</b> <sup>[b]</sup>	-Gly-OMe (5d)	- <i>t</i> Bu ( <b>6b</b> )	51
7 q <sup>[b]</sup>	-(CH <sub>2</sub> ) <sub>2</sub> OH (5k)	-CH <sub>2</sub> CO <sub>2</sub> $t$ Bu (6d)	40

[a] Reaction conditions: methanol as solvent, room temperature, 1 day reaction time. Bn=benzyl, cHx=cyclohexyl. [b] Instead of 10-undecenoic acid **2**, 3-butenoic acid **2a** was used. cedure starting from  $\gamma$ -aminobutyric acid (GABA). To show the simplicity of the synthesis of isonitriles from primary amines, **5c** was converted to the corresponding *ortho*-nitrobenzyl isonitrile **6e** in a two-step synthesis with an overall yield of 75%.<sup>[15]</sup> The Ugi-4CR with **5c** and **6e** gave the  $\alpha,\omega$ diene monomer **7d** with a yield of 57%. All these products were extensively characterized by TLC, NMR spectroscopy, and fast atom bombardment (FAB) mass spectrometry. <sup>1</sup>H and <sup>13</sup>C NMR spectra showed double signals, derived from mixtures of *cis/trans*-amide-containing products.

In consideration of sustainability, the use of amino acids, as well as peptides, could be beneficial. Thus, Ugi-4CRs were also carried out with amino acid methyl ester derivatives of glycine 5d, L- and D-alanine 5e and 5f, L-valine 5g, L-phenylalanine 5h, L-serine 5i, and the tert-butyl ester of glycine 5j. For these compounds, the yields of the obtained Ugi-4CR products 7e-7m were in all cases above 45% and reaching up to 69% (7i). For products 7l and 7m, the Ugi-4CRs were performed with the ester-functionalized isonitrile 6c derived from GABA. All amino acid-derived Ugi-4CR monomers were unambiguously characterized and it should be mentioned that the application of chiral amino acid derivatives 5e-5i led to the formation of diastereomers 7g-7k, which were inseparable by column chromatography on silica gel. These diastereomers with additional cis/transamide bonds showed complex <sup>1</sup>H and <sup>13</sup>C NMR spectra. Nevertheless, in combination with FAB mass spectrometry, the structure of these  $\alpha, \omega$ -diene monomers was also established. Based on the result that L-serine methyl ester with an unprotected hydroxyl group could be applied successfully, two additional examples with ethanolamine 5k were performed to obtain  $\alpha, \omega$ -diene Ugi-4CR products **7n** and **7o** in yields of 54 and 29%, respectively.

In the two final examples, the Ugi-4CR monomers **7p** and **7q** were synthesized by using 3-butenoic acid **2a** as an unsaturated short-aliphatic-chain carboxylic acid. This was to test if a shorter terminal double bond, which is located closer to the carbonyl group, would have a negative influence on the ADMET and/or the thiol–ene polymerization in comparison to 10-undecenoic acid derived  $\alpha,\omega$ -dienes.

All Ugi-4CR monomers were obtained as yellow or light brown oils in moderate to good yields. The creation of this small library of monomers by applying **2** and **4** clearly demonstrates the high versatility in the synthesis of  $\alpha,\omega$ -diene Ugi-4CR products by using different types of primary amine and isonitrile. Moreover, the application of functionalized amines and isonitriles provides countless possibilities for post-modification of the side chains of the monomers and polymers.

Subsequently, the behavior of the synthesized  $\alpha,\omega$ -unsaturated Ugi-4CR products in the ADMET polymerization was investigated. It is known that ruthenium-based metathesis catalysts (Grubbs-type catalysts) tolerate numerous functionalities, but it is also known that nitrogen-containing functionalities, such as amines, amides, and nitriles, can inhibit the catalysts and thus high catalyst loadings are required.<sup>[16]</sup> In a catalyst screening, the ruthenium-based olefin

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metathesis catalysts **C1** (Grubbs I), C2 (Grubbs II), C3 (Hoveyda-Grubbs II), and C4 (Zhan), as well as C5-C7 (M2,  $M3_1$ ,  $M5_1$ ) from the company Umicore, were tested for the polymerization of  $\alpha, \omega$ -diene monomer **7i** as a model for the prepared Ugi monomers (Scheme 3). Generally, all catalysts polymerized monomer 7i at temperatures of 80, 100, and 120°C for 4 h with catalyst loadings of 1.0 mol% under a continuous argon stream (Table 2). To avoid the wellknown double-bond isomerization of ruthenium-based metathesis catalysts during the metathesis process,<sup>[11]</sup> 1,4-benzoquinone (3.0 equiv according to catalyst amount) as additive can suppress the isomerization dramatically.<sup>[17]</sup> Under neat conditions at 80°C the precipitated polymers P1-P7 possessed molecular weights in a range between 3.6 (P1. Grubbs I C1) and 6.5 kDa (P7, Umicore M5<sub>1</sub> C7) and polydispersity indices (PDIs) between 1.6 and 2.4 measured by GPC. In repeated experiments similar results were obtained and it was decided to continue all following ADMET polymerizations with the most active catalyst C7.



Scheme 3. a) ADMET polymerization of Ugi-4CR product 7i and b) the tested catalysts (Cy=cyclohexyl, Mes=mesityl).

Furthermore, the polymerization with increased temperatures was investigated and it was found that at 100 °C (P8) slightly higher molecular weights (>7.0 kDa) were obtained, whereas at 120°C (P12) molecular weights decreased again. The reason for this seems to be the fast decomposition of C7 at this high temperature. Moreover, the application of different solvents in the ADMET polymerization was investigated. It was observed that under neat conditions the efficiency of stirring is strongly limited within a few minutes after addition of C7, and thus further polymerization is retarded. Different concentrations of xylene as solvent were tested at 100 (P9-P11) and 120 °C (P13-P15). A remarkable increase of the molecular weight up to almost 10.0 kDa (P9) was observed upon applying a concentrated xylene solution (2.6 mol L<sup>-1</sup>) at 100 °C with no significant change of the PDI. The use of more diluted xylene solution tends to result in lower molecular weights (P10 and P11). The results of the ADMET polymerization at 120 °C showed a similar tendency, but the molecular weights of between 4.8 and 8.0 kDa of the precipitated polymers were significantly

Table 2. Results of catalyst, temperature, and xylene concentration screening in ADMET polymerization with Ugi-4CR product  $7i.^{\rm [a]}$ 

				*	
Polymer	Catalyst type	Concentration of xylene $[mol L^{-1}]$	Т [°С]	$M_{ m n}$ $[ m gmol^{-1}]^{[ m b]}$	PDI $M_{\rm w}/M_{\rm n}^{\rm [b]}$
P1	C1	neat	80	3600	1.74
P2	C2	neat	80	3800	1.82
P3	C3	neat	80	5700	1.72
P4	C4	neat	80	4650	1.64
P5	C5	neat	80	5750	2.38
P6	C6	neat	80	4100	1.69
P7	C7	neat	80	6500	1.86
P8	C7	neat	100	7050	1.98
P9	C7	2.60	100	9900	1.86
P10	C7	1.04	100	8450	1.92
P11	C7	0.52	100	7100	1.93
P12	C7	neat	120	6750	1.83
P13	C7	2.60	120	7950	1.98
P14	C7	1.04	120	4950	2.02
P15	C7	0.52	120	4800	2.07

[a] Reaction conditions: catalysts **C1–C7** (1.0 mol%), 1,4-benzoquinone (3.0 mol%), Ar-purged, 4 h reaction time. [b]  $M_n$  and PDI of the precipitated monomer.

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lower (**P13–P15**). The PDIs of all polymerizations performed with **C7** were between 1.8 and 2.1. Based on these first screening experiments it seemed that optimal results in ADMET polymerizations of these rather challenging monomers were achieved by using catalyst **C7** at 100 °C in concentrated xylene solutions. These results were then tested in ADMET polymerizations with other Ugi-4CR monomers.

Subsequently, the ADMET polymerization with  $\alpha,\omega$ diene monomer **7a** derived from benzylamine was investigated under the optimized conditions at 100 °C (Scheme 4). Surprisingly, the obtained polymers (**P16–P21**) offered significantly higher molecular weights in a range between 7.5 and 18.4 kDa measured by GPC (Table 3). In contrast to the ADMET polymers derived from **7i**, in which the highest



Scheme 4. ADMET polymerization of Ugi-4CR products 7.

Table 3. Selected GPC results of ADMET polymerization with Ugi-4CR products  $\mathbf{7}^{[a]}$ 

Polymer	Monomer	Concentration of	T	$M_{\rm n}$	PDI
			ĮΟ	[giiloi ]	1 <b>v1</b> <sub>W</sub> /1 <b>v1</b> <sub>n</sub>
P16	7a	neat	100	10400	2.43
P17	7a	2.70	100	12700	2.66
P18	7a	1.08	100	10500	2.58
P19	7a	0.54	100	18400	2.83
P20	7a	0.36	100	11 500	1.79
P21	7a	0.27	100	7450	1.51
P22	7a	neat	120	10800	2.45
P23	7a	2.70	120	10500	3.02
P24	7a	1.08	120	15000	2.61
P25	7a	0.54	120	13 500	3.01
P26	7 f	neat	100	2950	1.56
P27	7 f	2.95	100	2950	1.54
P28	7 f	1.18	100	4150	1.73
P29	7 f	0.59	100	4250	1.74
P30	7 f	0.39	100	5000	1.90
P31	7 f	0.30	100	4100	1.71
P32	7b	neat	100	7450	1.75
P33	7c	neat	100	5400	1.52
P34	7 d	neat	100	5900	1.59
P35	7g	neat	100	14450	1.44
P36	7k	neat	100	no polymer	
P37	71	neat	100	28 800	1.74
P38	7m	neat	100	7550	1.67
P39	7p	neat	100	no polymer	
				1 2	

[a] Reaction conditions: catalyst **C7** (1.0 mol%), 1,4-benzoquinone (3.0 mol%), Ar-purged, 4 h reaction time. [b]  $M_n$  and PDI of the precipitated monomer.

molecular weight polymer was obtained in a concentrated xylene solution (P9), here more diluted solutions gave the better results. The polymer derived from a solution of 7a in xylene (P19) with a concentration of  $0.54 \text{ mol } \text{L}^{-1}$  gave the highest molecular weight with 18.4 kDa. Under neat conditions and concentrated xylene solutions, polymers were also obtained with considerable molecular weights over 10 kDa (P16-P18). More diluted solutions ended up with significantly lower molecular weight polymers (P20 and P21) with low PDIs. It thus seems that the side-chain moiety derived from the primary amine has a strong influence on the behavior of the ADMET polymerization. The benzyl group of 7a is obviously better tolerated than the L-valine methyl ester moiety in 7i. Probably, the unfunctionalized benzyl group has no interactions with the ruthenium catalyst, whereas the methyl ester group of L-valine could have a negative influence on the catalyst.

Finally, a test series in the ADMET polymerization of **7a** was accomplished at 120 °C (**P22–P25**). Here, the highest molecular weight polymer was achieved in a xylene concentration of  $1.08 \text{ mol L}^{-1}$  with 15.0 kDa. In all cases the measured PDIs were rather high up to a value of  $\approx 3.0$ . All experiments were repeated and gave identical results.

To further study the ADMET polymerization in xylene solutions,  $\alpha,\omega$ -diene Ugi-4CR monomer **7f** derived from glycine methyl ester **5d** and *tert*-butyl isonitrile **6b** were polymerized at 100 °C. The achieved polymers **P26–P31** all exhibited low molecular weights between 3.0 and 5.0 kDa with PDIs ranging from 1.5 to 1.9. The maximum molecular weight was also obtained at a low concentration of 0.39 mol L<sup>-1</sup>.

To summarize, it seems that the ADMET polymerization is strongly affected by the Ugi-4CR monomer structure. It is clear that the structures of amine and isonitrile moieties play an important role in the activity of catalyst **C7**. Moreover, the solubility of the different monomers will have a significant effect on the polymerization outcome. Thus, a generalization of the ADMET polymerization conditions is impossible and each monomer has to be optimized separately.

Nevertheless, all three tested monomers 7a, 7i, and 7f were successfully polymerized by ADMET polymerization to generate a new class of  $\alpha$ -alkylcarbamoyl-substituted polycarboxamides. Furthermore, the polymerization behavior of other synthesized a, w-diene Ugi-4CR monomers was investigated. In all following procedures, the ADMET polymerizations were tested under neat conditions at 100°C with 1.0 mol % of Umicore catalyst  $M5_1$  (C7). Monomer 7b, derived from para-methoxybenzylamine 5b and tert-butyl isonitrile 6b gave polymer P32 with a molecular weight of 7.5 kDa and a PDI of 1.8 determined by GPC. Monomers 7c and 7d with ortho-nitrobenzylamine moieties in the side chain were also polymerized successfully with C7 to obtain P33 (5400 kDa) and P34 (5900 kDa), respectively. These examples show the high functional-group tolerance, in this case nitro groups, of ruthenium-based catalysts. L-Alanine methyl ester derived monomer 7g was then polymerized to give poly-1-(alkylcarbamoyl) carboxamide P35 with a molecular weight of 14.5 kDa. In contrast, L-serine methyl ester derived monomer 7k could not be polymerized by ADMET and resulted only in dimers and trimers. The reason for this seems to be the primary hydroxyl group of serine. It is known that primary alcohols inhibit the ruthenium-based olefin metathesis catalysts during the ADMET process.<sup>[18a,b]</sup> Higher catalyst loadings might deliver better results, but would make the ADMET polymerization less useful and quite expensive. Recently, we demonstrated that secondary alcohols are much better tolerated by the ruthenium catalysts.<sup>[18c]</sup> Thus,  $\alpha, \omega$ -diene monomers with primary hydroxyl groups in the side chain might have to be protected for a successful application in the ADMET polymerization. Surprisingly, monomer 71 with two methyl ester functionalities in the side chain gave polymer P37 with a high molecular weight of almost 29.0 kDa, whereas monomer 7m with almost identical structure (one methyl ester is substituted by a tert-butyl ester) resulted in polymer P38 with a low molecular weight of 7.5 kDa. There is no explanation for these dramatic differences in molecular weights and repetitions gave similar results. Several factors, including the functionalgroup tolerance of the catalysts, tendency for ring formation, crystallization behavior of both monomers and polymers, and many other factors, will influence these ADMET polymerizations and make their outcome quite unpredictable. Nevertheless, these experiments clearly show that ADMET of the prepared Ugi monomers is possible and that this strategy can lead to structurally highly diverse polyamides.

Finally, monomer **7p** derived from 3-butenoic acid **2a** was tested in ADMET polymerization to determine if there is a different behavior in the reaction due to the short-chain  $\alpha, \omega$ -diene. As expected, the polymerization failed and only dimers and trimers were obtained (**P39**). The explanation for this is most likely the known negative neighboring group effect (NNGE)<sup>[19]</sup> because the double bond of the 3-butenoic acid moiety and the amide group are only separated by one methylene group. The amide group can act as a Lewis base and coordinate to ruthenium, and thus the inhibition of the catalyst is the consequence. A possible way to polymerize monomer **7p** could be the use of the thiol–ene addition polymerization instead of ADMET.

More information about the degree of polymerization (DP) of the investigated polymers was obtained by NMR spectroscopy because no suitable standards are available for GPC calibration for these novel polymers. The determination of DPs through direct correlation of integrals by <sup>1</sup>H NMR spectroscopy was not possible because the terminal double bonds were not observed, even in high enlargement. A very useful approach to determine the DP more exactly could be the addition of methyl 10-undecenoate 8 as chain stopper to prepare defined telechelic polymers. A suitable monomer for this experiment was 7b derived from para-methoxybenzylamine **5b**. The methoxy group of **7b** is very sig- MeO<sub>2</sub>C nificant in the <sup>1</sup>H NMR spectrum with a highly distinctive singlet signal at 3.77 ppm (Figure 1). Moreover, the methyl ester signal of chain stopper 8 appears as a singlet at 3.67 ppm. On the assumption that 8 incorporated completely



Figure 1. <sup>1</sup>H NMR spectra (CDCl<sub>3</sub>, 300 MHz) of monomer **7b**, polymer **P32**, and polymer with chain stopper **P40**.

in the ADMET polymerization with **7b**, more detailed information of the DP and consequently molecular weight could be obtained by integral correlation of the mentioned signals. The ADMET polymerization of  $\alpha,\omega$ -diene monomer **7b** was thus performed under neat conditions at 100 °C with different ratios of **8**, ranging from 5.0 to 30.0 mol%, to generate telechelic polymers **P40–P43** (Scheme 5, Table 4). By correlation of the terminal methyl ester signals with the methoxy group signals of the synthesized telechelic poly-1-(alkylcarbamoyl) carboxamides, the DPs and molecular weights of **P40–P43** were determined. As an example, the <sup>1</sup>H NMR spectrum of **P40** shows the dominant methyl ester signal at



Scheme 5. ADMET polymerization with monomer **7b** and methyl 10-undecenoate **8** as a chain stopper.

Table 4. GPC results of ADMET polymerization with Ugi-4CR product 7b and different amounts of chain stopper  $8^{[a]}$ 

Polymer	Amount of chain stop- per [mol %]	Degree of polymerization (DP)	$M_{\rm n}$ (calc.) $[{\rm g}{ m mol}^{-1}]^{[{ m b}]}$	$M_{\rm n}$ $[\rm gmol^{-1}]^{[b]}$	PDI $M_{\rm w}/M_{\rm n}^{\rm [b]}$
P40	30	≈13	7200	4450	1.99
P41	20	$\approx 26$	14050	6400	1.82
P42	10	$\approx 41$	22 000	7150	1.77
P43	5.0	$\approx 76$	40 400	7900	1.60

[a] Reaction conditions: catalyst **C7** (1.0 mol%), 1,4-benzoquinone (3.0 mol%), Ar-purged, T=100 °C, 4 h reaction time. [b]  $M_n$  and PDI of the precipitated monomer.

3.67 ppm in comparison to monomer **7b** and polymer **P32** (Figure 1). These results (Table 4) indicate that the molecular weights determined by GPC are underestimated in all cases. The NMR-based calculations indicated remarkable molecular weights ranging from 7.2 kDa (**P40**, 30 mol % **8**) up to  $\approx 40.0$  kDa (**P43**, 5.0 mol % **8**).

Figure 1 displays the <sup>1</sup>H NMR spectra of monomer **7b**, the ADMET polymer P32 derived from it, and the corresponding telechelic polymer P40 (30 mol % 8). Monomer 7b clearly shows the protons of the terminal double bonds at  $\approx$ 5.00 and 5.80 ppm. In contrast, the signals of terminal double bonds of polymer P32 disappear completely and a new multiplet signal is visible at  $\approx 5.40$  ppm, which corresponds to internal double bonds. The fact that in polymer P32 no terminal double bonds are detected, even in enormous enlargement, suggests a higher molecular weight than 7.5 kDa as determined by GPC. As mentioned above, telechelic polymer P40 exhibits, in addition to the methoxy group signal, a significant methyl ester singlet at 3.66 ppm, derived from chain stopper 8. Due to the fact that both signals are well separated and no other proton signals appear in this region, the possibility to determine the DP through integral correlation is indicated. Nevertheless, it should be mentioned that macrocycle formation might take place, which would lead to a misinterpretation of these results. However, macrocycle formation should be minimal, especially under bulk conditions and with large amounts of monofunctional monomer present. Thus, we can indeed assume that the GPC molecular weights of these polymers are underestimated.

Finally, all new polymers were characterized by DSC (Table 5). For all polymers, no melting points were detected, but glass transition temperatures  $(T_g)$  in a range between -22 (**P38**) and 23 °C (**P35**) were measured. It is clear that the  $T_g$  strongly depends on the side-chain structures derived from the primary amine and the isonitrile. Similar  $T_g$  values of -1.4 and 0.2 °C were detected in polymers **P19** (derived from benzylamine) and **P32** (derived from *para*-methoxy-benzylamine), respectively, which possess related structures. The amino acid ester derived polymers **P14** (derived from L-valine methyl ester) and **P27** (derived from glycine methyl ester) showed slightly decreased  $T_g$  values of -3.1 and -8.8 °C, respectively. An exception was observed in polymer

Table 5. Selected DSC results of ADMET polymers derived from Ugi-4CR monomers.

Polymer	Glass transition midpoint [°C]		
P19	-1.4		
P32	0.2		
P33	36.2		
P34	22.1		
P35	22.9		
P14	-3.1		
P37	-11.5		
P38	-21.9		
P27	-8.8		

**P35** (derived from L-alanine) with a higher  $T_g$  of 22.9 °C. Furthermore, polymers **P37** and **P38**, derived from glycine methyl and *tert*-butyl ester, as well as methyl ester functionalized  $\gamma$ -aminobutyric acid as the isonitrile compound, presented low  $T_g$  values of -11.5 and -21.9 °C, respectively. Also, the *ortho*-nitrobenzylamide-substituted polymers **P33** and **P34** exhibited higher  $T_g$  values of 36.2 and 22.1 °C, respectively, but no melting points were observed.

At length, three monomers of the synthesized Ugi products were chosen to be polymerized through thiol–ene addition polymerization to establish an alternative polymerization pathway for these  $\alpha, \omega$ -diene monomers. The radical thiol–ene addition polymerization of the renewable Ugi monomers resulted in partly renewable novel polyamides by a very simple and transition-metal-free procedure. The comparison and the discussion of reaction conditions of ADMET and thiol–ene polymerization for the syntheses of a number of biodegradable polymers had already been studied in our group.<sup>[9b]</sup> Therefore, we performed the polymerizations of the Ugi products **7a**, **7i**, and **7p** by UV-initiated thiol–ene addition polymerization with butane-1,4-dithiol **9** and 2,2-dimethoxyphenyl acetophenone (DMPA) as photoinitiator (Scheme 6).<sup>[20]</sup>

For this polymerization procedure, a small amount of solvent (THF) was necessary to allow stirring of the reaction



Scheme 6. Thiol–ene addition polymerization of Ugi-4CR monomers 7a, 7i, and 7p.

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magnetically because of the high viscosity. Polymers **P44** and **P45** exhibited molecular weights of about 7 and 9 kDa, which are acceptable for some applications (Figure 2a, Table 6). Compound **P46**, which offered the lowest molecular weight of about 3 kDa, could not reach a higher molecular weight, probably because the olefin functionality is located too close to the bulky side groups at which the approach of a thiol compound was sterically hindered. Because a similar behavior with only low molecular weight reached for this monomer was also observed by ADMET, this monomer might not only be influenced by the negative neighboring group effect in ADMET, but also by other factors such as a high tendency of cyclization. <sup>1</sup>H NMR analyses of the polymers proved the expected structures. Furthermore, we



Table 6.	GPC calculation	results of thiol-ene	polymers	P44-P46. <sup>[a]</sup>
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Polymer	Monomer	$M_{\mathrm{n}}$ [g mol <sup>-1</sup> ] <sup>[b]</sup>	PDI $M_{\rm w}/M_{\rm n}^{\rm [b]}$	Glass transition midpoint [°C]
P44	7a	8900	1.7	1.4
P45	7i	7300	1.6	9.6
P46	7 p	3100	1.5	7.7

[a] Reaction conditions: butane-1,4-dithiol **9** (1.0 equiv), DMPA (5.0 mol%), THF, Ar-purged, room temperature, 2 h reaction time. [b]  $M_n$  and PDI of the precipitated polymers.

also analyzed the thermal properties of the thiol-ene polymers by DSC (Figure 2b).

None of the samples exhibited any melting transitions on the second scan and only glass transitions were observed.

> When we consider the structure of the unsaturated monomers, clearly the existence of the bulky side groups prevents the polymer chains from getting into order, namely crystallization, and amide hydrogen atoms that are able to form hydrogen bridges remain hidden behind bulky cycloaliphatic and tert-butyl groups. Nevertheless, the slight shift of glass transition temperatures can be related to the size of those bulky groups. For instance, the lowest  $T_{\sigma}$  (P44) could be attributed to both cycloaliphatic and phenyl bulky groups located on the sides of the main chain. Nevertheless, P45 and P46, which have less pronounced bulky groups, exhibit higher  $T_{\rm g}$  values of 9.6 and 7.7 °C, respectively (Table 6).

> As an application of substituted polyamides derived by Ugi reactions, we tested the cleavage of the photolabile group of ortho-nitrobenzyl polymers P33 and P34 by irradiation. Sung et al. showed in 2008 the cleavage of ortho-nitrobenzylamides in small molecules derived from Ugi reactions.<sup>[21]</sup> In a first try, a solution of P33 in a mixture of methanol and THF (1:1) was irradiated with UV light at  $\lambda = 254$  nm for approximately 2 days (Scheme 7). Unfortunately, only a low level ( $\approx 15\%$ ) of cleaved polymer P47 was detected by <sup>1</sup>H NMR spectroscopy. In an-

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Scheme 7. Photolytic cleavage of *ortho*-nitrobenzylamide-substituted polymers **P33** and **P34** to obtain monosubstituted polymers **P47** and **P48**.

other test, the solution of **P33** was left outside to be irradiated by normal sunlight. After 5 days during a sunny period in springtime, complete cleavage was observed by <sup>1</sup>H NMR spectroscopy after precipitation in hexane (Figure 3). Due



Figure 3. <sup>1</sup>H NMR spectra (CDCl<sub>3</sub>, 300 MHz) of polymer **P33** not treated with light and sunlight-irradiated polymer **P47** after 5 days.

to this encouraging result, polymer **P34** was also irradiated with sunlight under the same conditions. A high conversion was also detected after 5 days for this reaction. The problem of the obtained polymer **P48** was the complete insolubility in all common solvents, as is known for polyamides. Polymer **P48** was partially soluble in CDCl<sub>3</sub> and analysis by <sup>1</sup>H NMR spectroscopy showed minor signals of the aromatic residue.

To analyze the thermal behavior, DSC thermograms of all four polymers were measured. The nonirradiated polymers **P33** and **P34** exhibited no defined melting points ( $T_m$ ), but  $T_g$  values at 36.2 (**P33**) and 22.1 °C (**P34**; Table 5). After light irradiation, the polymers **P47** and **P48** showed completely different thermal properties. The DSC analysis indicated no  $T_g$ , but clear melting endotherms at  $T_m=332.2$ (**P47**) and 304.5 °C (**P48**; Figure 4). Moreover, the thermogram of **P33** showed a strong exothermic signal starting at 225 °C and ending at 290 °C. Probably at this temperature



Figure 4. DSC thermograms of polymers P33 and P47.

the *ortho*-nitrobenzyl group started to decompose. In fact, an additional recorded <sup>1</sup>H NMR spectrum of the thermally treated polymer **P33** showed that the *ortho*-nitrobenzyl groups, as well as the methyl ester functionalities, were destroyed completely. These results clearly demonstrate the change of properties by sunlight irradiation. After cleavage of the nitrobenzyl group the monosubstituted amide moiety can form hydrogen bonds and thus the resulting polymer exhibits a high melting point. After further optimization, such photoresponsive properties could be suitable for material coatings, ultraviolet lithography techniques, and other applications.

#### Conclusion

The Ugi reaction with castor-oil-derived 10-undecenal and 10-undecenoic acid with several primary amines and isonitriles led to the formation of a small library of different poly-1-(alkylcarbamoyl) carboxamides, a new class of highly substituted  $\alpha, \omega$ -diene amides. The behavior of these monomers was investigated in the ADMET polymerization, as well as in the thiol-ene addition polymerization. In a catalyst screening process, we observed that the highest molecular weights were obtained by applying the catalyst M5<sub>1</sub> from Umicore. Moreover, a temperature screening was performed and the best results regarding high molecular weights occurred at 100 °C. Furthermore, the application of ADMET polymerizations in xylene solutions gave positive results, but strongly depended on the structure of the monomer used. In addition to the ADMET polymerization, we demonstrated that the photoinitiated thiol-ene addition polymerization is also a very useful tool for the generation of highly substituted polyamides from Ugi  $\alpha, \omega$ -diene monomers in a transition-metal-free procedure. Finally, it was possible to demonstrate the cleavage of the ortho-nitrobenzyl functionality as an amide protecting group on polymers by irradiation with sunlight. After cleavage, the polymers exhibited a drastic change of their properties regarding solubility and thermal properties. These results indicate interesting application possibilities as photoresponsive materials.

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In summary, it can be said that the Ugi reaction with 10undecenoic acid and 10-undecenal as castor-oil-derived platform chemicals is a powerful approach in the synthesis of highly substituted  $\alpha, \omega$ -diene amide monomers, which can be successfully polymerized by applying the ADMET or thiolene addition polymerization.

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