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Polyamide Synthesis from 6-Aminocapronitrile, Part 1: *N*-Alkyl Amide Formation by Amine Amidation of a Hydrolyzed Nitrile

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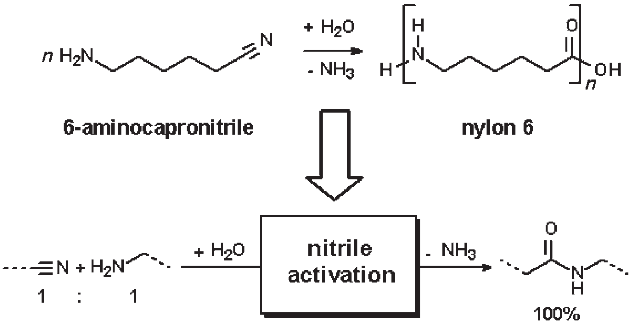
Abstract: The synthesis of *N*-hexylpentanamide from a stoichiometric amount of pentanenitrile and hexylamine has been studied as a model reaction for the synthesis of nylon-6 from 6-aminocapronitrile. The reaction was carried out under mild hydrothermal conditions and in the presence of a homogeneous ruthenium catalyst. For the mild hydrothermal conditions the presence of hexylamine distinctively increases the nitrile hydrolysis compared to the nitrile hydrolysis in the absence of hexylamine. Amine-catalyzed nitrile hydrolysis mainly produces the N-substituted amide. A clear product development is observed, consisting of first the terminal amide formation and second the accumulation of *N*-hexylpentanamide. With a maximum conversion of only 80 % after 18 h, the nitrile hydrolysis rate at 230 °C is still much too low for nylon-6 synthesis. Ruthenium dihydride phosphine was therefore used as a homogeneous catalyst, which significantly increases the nitrile hydrolysis rate. At a temperature of 140 °C and with only 0.5 mol % [$RuH_2(PPh_3)_4$] a 60 % nitrile conversion is already reached within 2 h. Initially the terminal amide is the sole product, which is gradually converted into *N*-hexylpentanamide. The reaction has a high initial rate, however, for higher conversions a strong decrease in hydrolysis rate is observed. This is ascribed to product inhibition, which results from the equilibrium nature of the reaction.

Keywords: amides · hydrolysis · nitriles · polymers · ruthenium

Introduction

Thanks to its excellent physical properties, nylon-6 is one of the most widely used engineering plastics. However, production of the monomer *ε*-caprolactam as the raw material is cumbersome and environmentally unfriendly.[1] Nylon-6 formation from 6-aminocapronitrile (ACN) as a monomer (Scheme 1) is an attractive alternative that has received considerable attention, especially from industry.[2] ACN can be prepared starting from butadiene through consecutive hydrocyanation and hydrogenation. So far, the knowledge about the chemistry involved for the combined nitrile hydrolysis and amine amidation of ACN is still limited and a better understanding of the fundamental aspects of each of the reaction steps involved is required to develop a viable process for the production of high-molecular-weight nylon-6 from ACN. The chemistry involved in the hydrolysis and the



Scheme 1. The essential chemistry of the nylon-6 synthesis from 6-aminocapronitrile.

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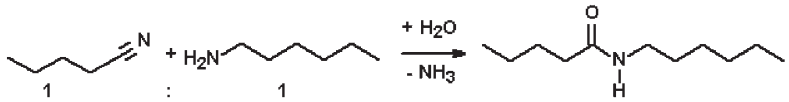
polycondensation of ACN is described by the reaction of equimolar amounts of an unactivated nitrile, a primary amine, and water resulting in the formation of an N-substituted carboxylic amide (Scheme 1). The process requires two chemical transformations: 1) the hydrolysis of the nitrile and; 2) the amidation of the amine.

Literature on the nitrile hydrolysis is dominated by studies on the selective formation of the terminal amide[3,4] and by studies on the mechanism of nitrile hydrolysis.[3v,w,5,6] Despite the potential of this transformation, the synthesis of *N*-alkyl amides from nitrile and amine reagents has obtained very little attention so far. Except for some specific dinitriles and acetonitrile,[7,8a] the combined hydrolysis–aminolysis reaction of a nitrile group with primary or secondary amines requires a catalyst to give a substituted amide and ammonia as a high yield product at mild temperature.[8,9] The most promising results have been observed with ruthenium and platinum catalysts.[8] Murahashi and co-workers could obtain high yields of N-substituted amides with different nitrile–amine combinations. However, this required a 24-hour reaction time at 160 °C with no less than 3 mol % of $[RuH_2(PPh_3)_4]$ and a solvent.[8b] De Benneville and co-workers demonstrated that an eight-hour reaction time at 150 °C is sufficient to obtain the desired product in 83 % yield by using H_2S as a catalyst.[8a] Although the reaction did not require a solvent, 25 mol % of the highly undesirable H_2S is needed. The best catalyst performance so far has been reported by Cobley and co-workers.[8c] With a catalyst loading 30-times lower than that for the ruthenium system, the homogeneous platinum complex used produced 89 % of N-substituted amide under the same conditions as used by Murahashi. Although promising, it is clear that these yields are far from sufficient for nylon-6 synthesis since complete conversion of the nitrile and the amine functionalities, and complete selectivity towards the corresponding *N*-alkylamides are prerequisites for the formation of high-molecular-weight polyamides.

As a model reaction for the nylon-6 synthesis out of 6-aminocapronitrile, in this contribution we study the synthesis of *N*-hexylpentanamide out of a stoichiometric amount of pentanenitrile and hexylamine. The objective is to elucidate the feasibility and bottlenecks for high-yield *N*-alkyl amide synthesis from an aliphatic, primary amine and an aliphatic nitrile. The combined nitrile hydrolysis and amidation has been studied, both without a catalyst under mild hydrothermal conditions and with $[RuH_2(PPh_3)_4]$ as a catalyst at lower temperatures.

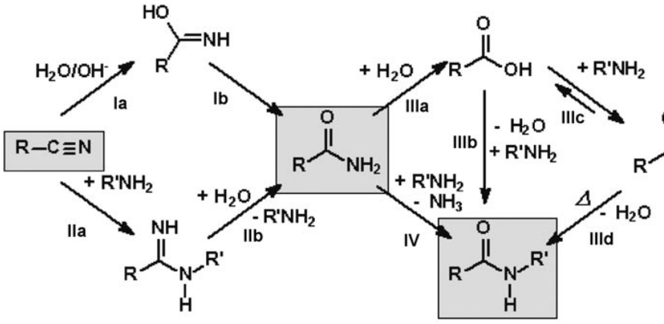
Results and Discussion

To ensure that the model for the combined hydrolysis and polycondensation of ACN to nylon-6 is realistic, we restricted ourselves to a solvent-free system consisting of equimolar amounts of *n*-pentanenitrile and *n*-hexylamine to form *N*-hexylpentanamide (Scheme 2). The risk of phase separation with these aliphatic substrates was avoided by limiting the amount of water used to a maximum of ten equivalents.



Scheme 2. Overall reaction for the synthesis of *N*-hexylpentanamide from pentanenitrile and hexylamine.

Nitrile activation by using hydrothermal conditions: Since hydrothermal nitrile hydrolysis is a well-known process in organic chemistry,[11] we first studied the potential of this process for the formation of nylon-6 by using pentanenitrile and hexylamine as model reagents (I, Scheme 3). Figure 1 shows the conversion–time history for the reaction of pentanenitrile with ten equivalents of water at 230 °C.[12] For the nitrile–water mixture only, pentanenitrile was hardly hydrolyzed. This hydrolysis behavior resembles the literature observations. For example, a reaction temperature of 250 °C resulted in only a 20 % propionitrile conversion in a large excess of water,[5b] while temperatures of at least 300 °C were required to obtain complete nitrile hydrolysis under hydrothermal conditions.[5,10] Adding a primary amine (*n*-hexylamine) to the system clearly promotes the nitrile hydrolysis and a steadily and significantly increasing conversion of pentanenitrile with time is observed (Figure 1). Nev-



Scheme 3. Possible reaction paths for the synthesis of *N*-hexylpentanamide from pentanenitrile, with R: C_4H_9 and R′: C_6H_{11}.

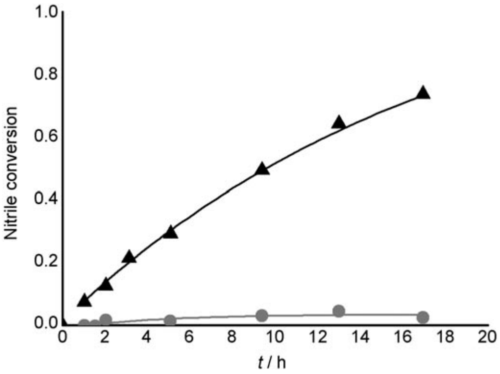


Figure 1. Conversion–time history for the pentanenitrile hydrolysis without hexylamine (●) and with a stoichiometric amount of amine (▲), at 230 °C.

ertheless, still rather high temperatures are required. A temperature reduction to 160 °C results in only 8 % of hydrolyzed pentanenitrile after 22 h. Although increasing the temperature seems the most obvious choice to increase the conversion, a much higher temperature is no option when this process is used for nylon synthesis. A recent study on the thermal cyclization of 6-aminocaproic acid amide showed a dramatic drop in the selectivity for ε-caprolactam at high temperature as a result of amine disproportionation yielding secondary and tertiary amines.[10] Although amine disproportionation poses no real threat in organic synthesis, for polycondensations, even small amounts of secondary amines lead to branches and loss of selectivity. Moreover, the stoichiometric balance is disturbed, which is deleterious for the required high molar mass.[13]

Hydrolysis increase due to the reactant hexylamine is interesting, as nitrile hydrolysis without the use of additives requires high reaction temperatures. Since nitrile hydrolysis is known to be both acid- and alkaline-catalyzed,[6f,g] the distinct improved hydrolysis rate of pentanenitrile is most probably due to the basicity of the amine (I, Scheme 3). The formation of ammonia counterbalances the consumption of amine for the combined nitrile hydrolysis and amine amidation.[5c] The result is a more constant nitrile hydrolysis rate. When primary (or secondary) amines are used, another plausible origin for the increased reaction rate would be that the amine acts as a catalyst by formation of an amidine intermediate.[14] In agreement with the observed composition development, the hydrolysis of the amidine should lead to a terminal amide and not directly to an N-substituted amide as *n*-hexylamine is a better leaving group than ammonia (route II, Scheme 3). Hence, the direct formation of N-substituted amides through the hydrolysis of an amidine is excluded.

The main products of the nitrile hydrolysis in the presence of amine are the corresponding terminal amide, pentanamide, and the *N*-alkyl amide, *N*-hexylpentanamide (Figure 2). Note that the reactions were performed in a closed system, so the generated NH_3 was not removed. No loss of selectivity is observed for pentanenitrile and hexylamine, with a maximum error in the total mass balance of 2 %. The maximum amount of the corresponding carboxylic acid formed is less than 1 % based on the initial amount of nitrile and is only detected at higher conversions. This is remarkable as the major product of the nitrile hydrolysis at hydrothermal conditions in the absence of amine is the corresponding carboxylic acid,[5a–c,f] and hydrolysis of nitriles into the terminal amide requires the use of a selective catalyst.[6a,15] The small amount of carboxylic acid formed in the reaction of pentanenitrile, *n*-hexylamine and water can be rationalized by assuming a relatively low hydrolysis rate of the pentanamide compared to a fast consumption rate of the formed carboxylic acid by acylation of hexylamine. This difference in the reaction rates prevents the built up of appreciable amounts of carboxylic acid, as shown by Scheme 3. As demonstrated in Figure 2a, the development of the product composition with increasing conversion shows a clear behavior. At the beginning of the reaction the terminal amide is the major product, after 25 % conversion, a selectivity of 90 % for *N*-hexylpentanamide is obtained. Although pentanamide remains present, it only contributes to less than 10 % of the total yield at higher conversions. An important conclusion that can be drawn from these results is that even without removal of the formed NH_3 the system has a strong thermodynamic preference for the formation of the N-substituted amide over the terminal amide and the carboxylic acid.

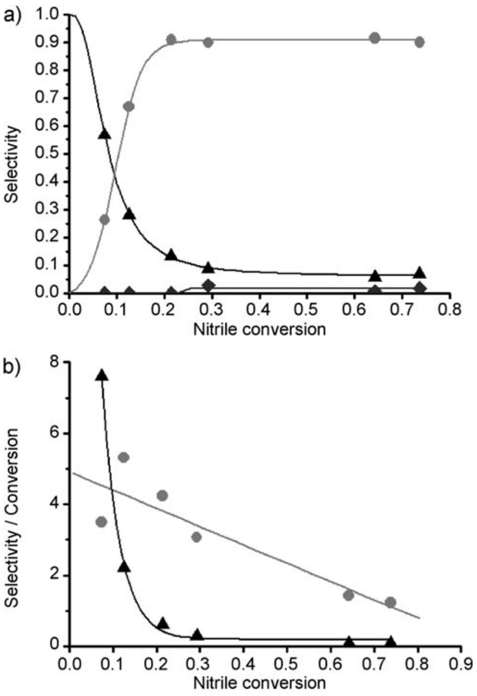


Figure 2. First- (a) and second-order Delplot (b) for the hydrothermal pentanenitrile hydrolysis in the presence of hexylamine, without NH_3 removal. Reaction products: Pentanamide (▲), *N*-hexylpentanamide (●), and pentanoic acid (◆).

Figure 2a is also considered as the first-rank Delplot, which allows the assignment of the reaction rank to the different products involved.[16] The initial selectivity of pentanamide tends to unity, which implies that the amide is the primary product of the reaction network. The zero selectivity for *N*-hexylpentanamide at nitrile conversions approaching zero shows that it is a higher-rank product. Figure 2b shows the second-rank Delplot for the pentanenitrile hydrolysis in the presence of hexylamine at 230 °C, which allows sorting of higher rank products in the reaction network.[16] As the *y* intercept for pentanamide in the secondary Delplot goes to infinity for zero conversion, the assignment of pentanamide as the primary product is confirmed. As *N*-hexylpentanamide has a finite, positive value of the *y* intercept, it is the product of the consecutive amidation of the terminal amide.[17] The observations correspond with a consecutive reaction mechanism, as shown in Scheme 3.[18]

Hexylamine amidation with pentanamide: To assess the feasibilities of routes III and IV in Scheme 3 and to get insight into the effect of water on the system, the *N*-alkyl amide formation from a terminal amide and a primary amine in the presence of water was studied separately by using the neat reaction of pentanamide with hexylamine. Although amine acylation is the most widely used method for preparing N-substituted amides,[15] the use of terminal amides as acylation source is hardly reported.[19,20] This is not surprising as the formation of amides by using amine amidation with carboxylic acids is already considered as a poor synthetic method.[15,21] Note that amides are even less reactive towards nucleophilic substitution than carboxylic acids. The two possible routes for the amine amidation with a terminal amide in aqueous environment are depicted in Scheme 3. The first step for reaction III is the hydrolysis of the amide to the carboxylic acid, followed by the formation of the ammonium salt. The ammonium salt dehydrates at high temperature. The direct amine amidation using a terminal amide (IV, Scheme 3) is mainly performed under dry conditions and requires some method of activation.[20b,d]

The results for the neat hexylamine amidation with pentanamide in the absence of water are collected in Figure 3a for 180 and 230 °C. As expected, the amidation rate at 180 °C is low. At this temperature it takes more than five hours to reach 80 % conversion. At 230 °C the initial rate is high and the same 80 % conversion is already reached within two hours. However, completion of the reaction does not occur as equilibrium seems to be reached. Preliminary experiments showed that stepwise removal of ammonia from the reaction mixture further increases the *N*-hexylpentanamide yield. Although no complete ammonia removal could be achieved with the setup used, the yield increased from 85 % without ammonia removal to 93 % with three ammonia removal cycles. The amine amidation rate with pentanoic acid is considerably higher than with pentanamide (Figure 3b). Within five hours a 95 % yield is reached at 180 °C, and at 230 °C the thermodynamic equilibrium of the system is already reached within one hour. This is in agreement with our observation that only a small amount of carboxylic acid is formed in the model reaction of pentanenitrile with hexylamine and water at high temperature.

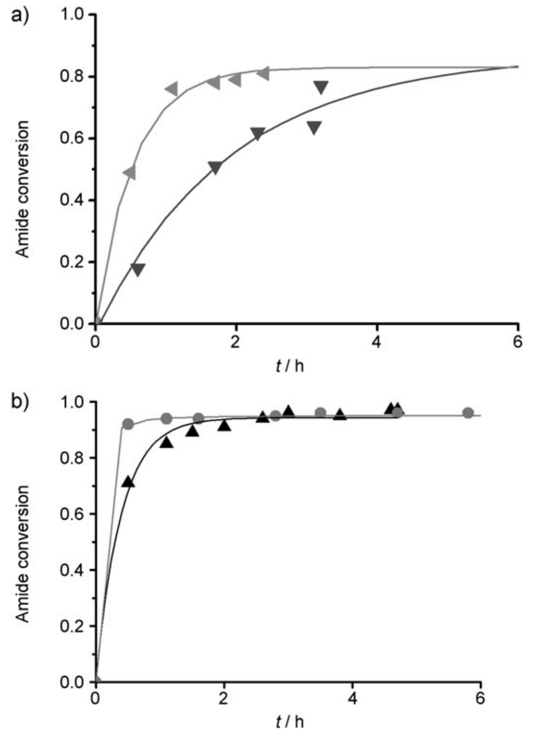


Figure 3. a) Hexylamine amidation with pentanamide performed at 180 °C (▼) and at 230 °C (◀); b) hexylamine acylation of *n*-hexylamine with pentanoic acid performed at 180 °C (▲) and at 230 °C (●). Closed system.

Figure 4 shows the results of the amidation of hexylamine with pentanamide, both dry[22] and in aqueous environment. *N*-hexylpentanamide and pentanoic acid comprise the total conversion of pentanamide and hexylamine, which excludes side reactions. The results demonstrate that water influences the amine amidation positively at higher conversion. For the water-free reaction conditions a 76 % conversion was

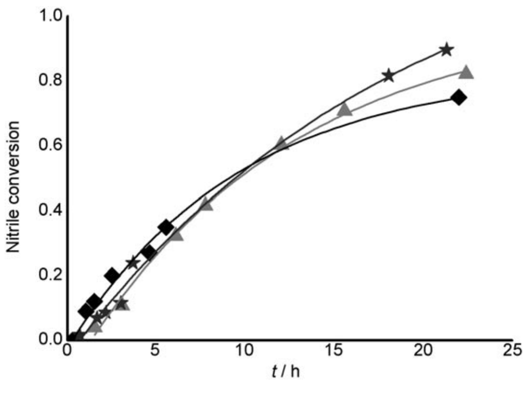


Figure 4. Conversion–time histories for the hexylamine amidation with a stoichiometric amount of pentanamide at 140 °C, comparison of the effect of water, in the absence of water (◆), 2 equiv of water (▲) and 10 equiv of water (*) compared to pentanenitrile (closed system).

reached, while with ten equivalents of water, over 90 % of amide was converted after 22 h at 140 °C. The formation of 1.5 % of carboxylic acid suggests that this increased conversion can be assigned to the formation of carboxylic acid as intermediate product, according to route III in Scheme 3. During the experiment with ten equivalents of water a maximum amount of 15 % of carboxylic acid was formed, which was subsequently consumed on progress of the reaction. Although hydrolysis of the amide to the corresponding acid does not proceed very fast, it definitely contributes to the increased *N*-hexylpentanamide yield, compared to the water-free system. Varying the amine concentration (1–8 equivalents) does not influence the amine amidation. This strengthens the possibility of *N*-hexylpentanoic amide formation via the pentanoic acid (III, Scheme 3), with amide hydrolysis being the rate determining step.

A preliminary conclusion: The observed phenomena for the synthesis of *N*-hexylpentanamide from pentanenitrile, *n*-hexylamine, and water under mild hydrothermal conditions can be summarized as follows. Nitrile hydrolysis requires harsh conditions,[5a,b] but the presence of the primary amine reduces the activation barrier for hydrolysis leading to considerably higher reaction rates at 230 °C. The time constant for the amine amidation is lower than the time constant for the nitrile hydrolysis. The terminal amide formed upon nitrile hydrolysis can either be directly amidated with hexylamine or first hydrolyzed to the corresponding acid. As the amide amination is not influenced by the amine, the product *N*-hexylpentanamide is probably mainly formed through the hydrolysis of the terminal amide (III, Scheme 3). This is supported by the formation of carboxylic acid for higher conversions, as the amidation rate is decreased as a result of a low amine concentration. However, the direct amidation of hexylamine with pentanamide can not be excluded. Ammonia removal during the amidation reaction proved to be cumbersome for the used setup. Nevertheless, partial ammonia removal already showed an improved performance. Nevertheless, the reaction rates and conversions obtained by hydrothermal nitrile hydrolysis and subsequent amine amidation are too low for the process to be useful for nylon-6 synthesis. In the next section, the results of a study on ruthenium-catalyzed nitrile hydrolysis and amine amidation will be discussed.

Ruthenium-catalyzed nitrile hydrolysis and amine amidation: The dimensionless concentration-time history for the solvent-free reaction of pentanenitrile with *n*-hexylamine and two equivalents of water, catalyzed by $[RuH_2(PPh_3)_4]$, at 140 °C, in a closed system, is shown in Figure 5 a. The ruthenium catalyst clearly has a strong accelerating effect on the nitrile hydrolysis compared to the hydrothermal hydrolysis. With only 0.5 mol % $[RuH_2(PPh_3)_4]$, 60 % conversion is already reached within two hours at 140 °C, while this requires 12 h at 230 °C for the uncatalyzed reaction. In analogy with the uncatalyzed reaction the terminal and coupled amide are the main products. The only reaction product up to a nitrile conversion of 60 % is the terminal amide (see Figure 5b). Distinct amounts of *N*-hexylpentanamide are only observed for high nitrile conversions, as is clearly demonstrated. The observed sequential process as depicted in Scheme 3 is even more pronounced for the ruthenium-catalyzed hexylamine amidation with hydrolyzed pentanenitrile than for the hydrothermal conditions. Although the same consecutive reaction steps are observed, a dramatic change in rate-determining step occurs. Whereas the nitrile hydrolysis is rate-limiting for the hydrothermal conditions, this step is effectively catalyzed by the ruthenium compound rendering the amidation reaction to be the rate-limiting step (Figure 5). An independent experiment has shown that $[RuH_2(PPh_3)_4]$ has no significant effect on the amine amidation rate.

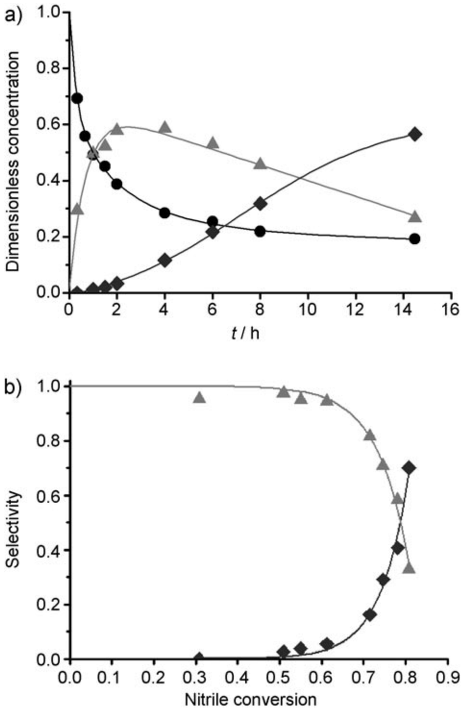


Figure 5. a) Concentration–time diagram for the $[RuH_2(PPh_3)_4]$-catalyzed (0.5 mol %) *n*-hexylamine amidation with pentanenitrile and 2 equivalents of water in a closed system. b) The corresponding selectivity–conversion plot: Normalized concentration pentanenitrile (●), pentanamide (▲), and *N*-hexylpentanamide (◆).

To asses the possible effect of the presence of amines on the reaction rate, the nitrile hydrolysis was also carried out in the absence of hexylamine. Pentanenitrile does not dissolve appreciably in water without amine present and a homogeneous system is required to properly compare the hydrolysis rate. Therefore the hydrolysis, both in the absence and presence of amine, was performed in dimethoxyethane. After two hours, at 140 °C, with 0.5 mol % of $[RuH_2(PPh_3)_4]$, 10 % conversion of pentanenitrile is obtained in the presence of *n*-hexylamine against 5 % conversion without amine. Although the hydrolysis rate is lower due to dilution and perhaps solvent effects, a clear increase in rate is observed for the experiment in the presence of *n*-hexylamine. There are various conceivable reasons for the increased nitrile hydrolysis in the presence of amines, the most probable one being that the amine acts as a cocatalyst, which promotes proton exchange that is required to liberate the formed amide from the catalytic site.[23] Another option might be the activation of the ruthenium complex by the substitution of one phosphine ligand by the amine, which results in a more open and more reactive complex.

Improving the ruthenium-catalyzed nitrile hydrolysis: It was found that the initial hydrolysis rate is dependent on the water concentration. When going from one to two equivalents of water, a clear increase in conversion could be observed. A further increase to ten equivalents resulted only in a slight increase in conversion and above ten equivalents, no further change in activity could be observed. At 140 °C, the initial rate is about a factor 1.4 higher when two equivalents of water are used instead of one equivalent.[24]

As shown in Figure 6, the ruthenium catalyst concentration has a strong effect on the final conversion level reached. However, a strong reduction in hydrolysis rate is observed at higher conversions for all catalyst concentrations ranging from 0.05 to 1.0 mol % (see below). On the other hand, with 2.5 mol % of ruthenium a 98 % nitrile conversion can be obtained, but for a viable process lower catalyst loadings are required. This reduction in hydrolysis rate is observed for the ruthenium-catalyzed hydrolysis of nitrile, both with and without amine present. However, the decrease of the nitrile hydrolysis activity is more pronounced in the presence of amine.

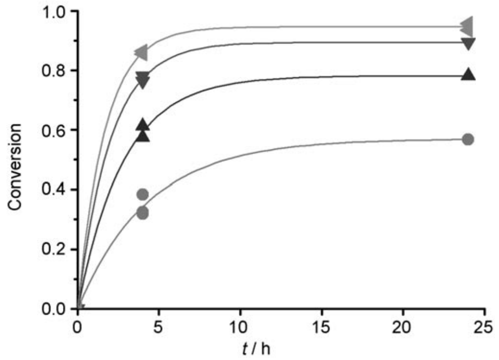


Figure 6. Nitrile conversion for the model reaction with 0.05 mol % (●), 0.2 mol % (▲), 0.5 mol % (▼), and 1.0 mol % (◀) [$RuH_2(PPh_3)_4$] in a closed system. The shown curves are only guides for the eye.

Figure 7 shows the conversion–time history of the nitrile hydrolysis with 0.5 mol % ruthenium catalyst at different temperatures. Figure 7 shows an increase of the final conversion with increasing temperature. After two hours of reaction at 180 °C the nitrile conversion exceeds 85 %, compared to a 70 % conversion at 160 °C for the same reaction time. Unfortunately, at temperatures higher than 160 °C, side reactions become significant. It was reported that ruthenium effectively catalyzes the formation of secondary and tertiary amines from primary amines at elevated temperatures.[25] Indeed, part of the discrepancy in amine conversion and *N*-hexylpentanamide yield corresponds well to the amount of dihexylamine formed during the reaction at temperatures higher than 160 °C. As mentioned before, for polycondensations even small amounts of secondary amines lead to branches and disturb the stoichiometric balance, which is detrimental for the required high molar mass of nylon-6.

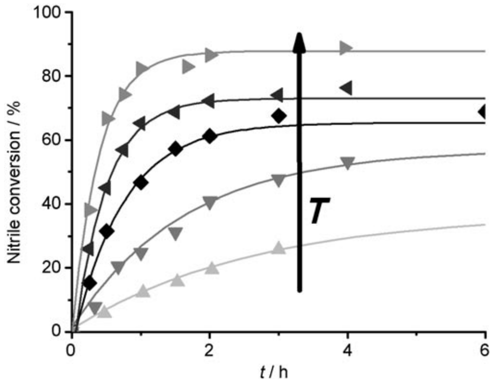


Figure 7. Nitrile conversion for the model reaction at different temperatures. T_r = 100 °C (▲), 120 °C (▼), 140 °C (◆), 160 °C (◀), 180 °C (▶), 0.5 mol % [$RuH_2(PPh_3)_4$] in a closed system.

The results collected in Figure 6 and Figure 7 clearly demonstrate that the nitrile conversion levels off in time. Plausible reasons for this deactivation can be either catalyst decomposition or the inhibition of the active metal species by the formed products. The addition of a mixture of nitrile, amine, and water to a mixture which had reacted for 19 h resulted in about 60 % hydrolysis of the extra added nitrile in an additional three hours. Hence, the observed renewed activity excludes significant decomposition of the active ruthenium species and indicates a reversible inhibition process. The reversible character of the activity decrease is also supported by the observation that a stepwise addition of the catalyst in time results in the same conversion compared to the experiment, for which the same total amount of catalyst is initially added. Hence, the process is hampered by product inhibition, a well-known phenomenon in catalysis.

To unravel the inhibition mechanism, the influence of the effect of ammonia, pentanamide, and *N*-hexylpentanamide on the hydrolysis activity was studied. Application of a partial ammonia pressure at the start of the reaction did not affect the hydrolysis activity. It is not surprising that ammonia has no effect, since the strong decrease of the hydrolysis activity is observed before appreciable amounts of N-substituted amides and ammonia are formed. The decrease of the catalyst performance upon addition of the pentanamide (Figure 8) is much more pronounced than the decrease that can be expected as a result of merely the dilution of the neat system as a result of the addition of pentanamide. Addition of *N*-hexylpentanamide was found to have a compara-

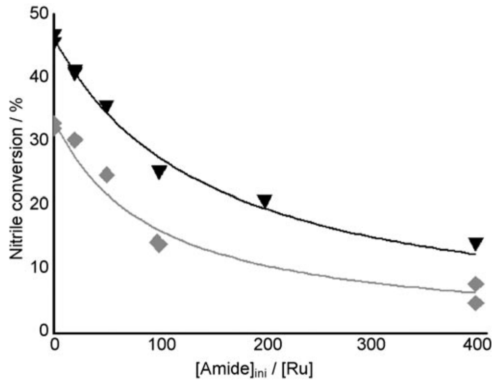


Figure 8. Observed reduction in nitrile conversion after 1 h reaction time with increasing initial amount of pentane amide added, both for a reaction mixture with (▼) and without (◆) *n*-hexylamine. With 0.5 mol% $[RuH_2(PPh_3)_4]$, $T = 140\,°C$ (closed system).

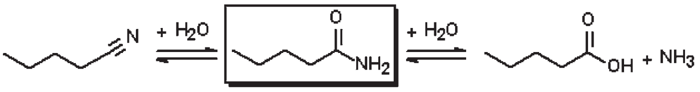
ble effect. So, the terminal and *N*-hexylpentanamide plays a dominant role in the reversible catalyst deactivation.[26]

Ruthenium-catalyzed amide dehydration and hydrolysis: Although amide functionalities are rather robust, hydrolysis into their corresponding carboxylic acids is a common transformation and terminal amides can even be dehydrated to their nitrile analogues. In Table 1 the results are collected for the stability of pentanamide at 140 °C against hydrolysis and dehydration as depicted by Scheme 4. As expected, pentanamide is stable for prolonged periods of time and the addition of water results in only a small amount of carboxylic acid formation.

Table 1. Pentanamide stability towards hydrolysis and dehydration.[a]

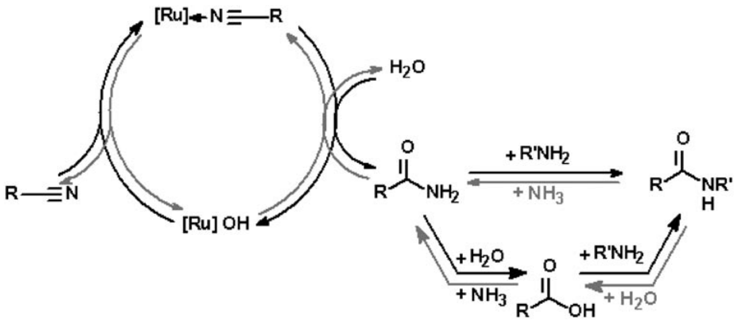
Entry	$[H_2O]$ [molar equiv]	$[RuH_2(PPh_3)_4]$ [mol%]	Y_{PN}[c] [%]	Y_{PA}[d] [%]
1	0[b]	–	0	0
2	0[b]	1	4	1
3	1	–	0	3
4	1	1	2	16
5	2	–	0	3
6	5	1	0	10
7	5	2	0	10

[a] 22 h and 140 °C. [b] Dried pentanamide used. [c] Yield of pentanenitrile. [d] Yield of pentanoic acid



Scheme 4. Equilibrium reactions for pentanamide.

As the amide competes with the nitrile for the coordination to the ruthenium metal, an equilibrium can also exist between a ruthenium nitrile species and a ruthenium amide. The role of amide dehydration as part of the nitrile hydrolysis mechanism has not been extensively studied, as dehydration is generally not observed.[5b,27] Nevertheless, the existence of an equilibrium is quite possible, as ruthenium phosphines are known to dehydrate amides in the absence of water, especially when the water that is formed is removed from the system, for example, by using urea.[28] With 1 mol% of $[RuH_2(PPh_3)_4]$ the formation of the corresponding nitrile as the dehydration product is indeed observed at 140 °C, see Table 1. The water formed due to the dehydration is partially involved in hydrolysis of the amide leading to some carboxylic acid formation. Even in the presence of one equivalent of water, some pentanenitrile is formed from the corresponding amide. Increasing the amount of water to ten equivalents is enough to make quantification of the dehydration impossible. These results demonstrate that the nitrile hydrolysis catalyzed by $[RuH_2(PPh_3)_4]$ is an equilibrium reaction (Scheme 5) and confirms that pentanamide coordinates competitively with nitrile onto the catalyst. Scheme 5 combines all the observations for the system consisting of a nitrile, a primary amine, and water with $[RuH_2(PPh_3)_4]$ as a catalyst precursor. The system is fully reversible and the products are in thermodynamic equilibrium under the conditions applied.



Scheme 5. Reaction scheme for the ruthenium-catalyzed synthesis of *N*-hexylpentanamide from pentanenitrile.

Conclusion

The synthesis of *N*-hexylpentanamide from pentanenitrile and hexylamine was studied at mild hydrothermal conditions and with the use of ruthenium catalysts. The reaction proceeds through two consecutive reactions that are independent of the use of a catalyst. The first reaction is the nitrile hydrolysis to the terminal amide, which is followed by amine amidation of the formed terminal amide. The presence of amine significantly increases the nitrile hydrolysis as compared to the nitrile hydrolysis without additional amine. Still, the hydrolysis remains the rate determining step in the hydrothermal system and the overall activity of the system is too low to be of practical use for the production of nylon polymers out of amino nitriles.

It was found that $[RuH_2(PPh_3)_4]$ effectively catalyzes the nitrile hydrolysis, but has no influence on the amine amidation. The desired reduction of the amount of catalyst results in a decrease of the final yield, which is caused by reversible product inhibition of the active species. Preliminary tests showed that the decrease in hydrolysis rate with lower catalyst loadings can partly be counterbalanced by using increased temperatures and removing ammonia. On the other hand, increased temperatures result in side reactions of the primary amine, which would result in a non-stoichiometric amount of functional groups in a polymerization reaction of ACN, and in branched and low-molar-mass nylon-6. Hence, although very useful for the organic synthesis of N-substituted amides from nitriles and amines, this ruthenium catalyst is not the most suitable for the direct polycondensation of amino nitrile monomers such as ACN to nylon-6. Other catalysts that are less prone to product inhibition and side reactions at high temperatures have been explored and the results are described elsewhere.[29]

Experimental Section

All reactions and manipulations involving ruthenium complexes were performed in an argon atmosphere by using standard Schlenk techniques or in a nitrogen-filled glove box, and the product mixtures were worked up in open flasks in air. The reaction products were identified by using ^{1}H NMR spectroscopy. Conversions of substrates and selectivities for product formation were determined by gas chromatography by using p-xylene as an internal standard. The product mixtures were analyzed by using a CP 9000 gas chromatograph (GC) equipped with a 30 m × 0.32 mm id, capillary CP volamine column and a FID detector. The sample was injected at 120 °C and after a stabilization temperature of 1 min the temperature was raised at 15 °C min^{-1} to 290 °C. All single-point experiments were performed in duplicate.

Hydrolysis experiments were performed in closed, stainless steel microreactors that contained glass inserts. These autoclaves, with 7-mL internal volume, were made in-house by the workshop of the Eindhoven University of Technology. Sealing during the reaction was ensured by using Kalrez o-rings, as these are resistant against the aggressive ammonia that was formed. The maximum operation temperature and pressure were 250 °C and 60 bar, respectively. The internal reactor temperatures were controlled within ± 2 °C by a heating mantle. Reaction mixtures were stirred with magnetic stirring bars.

Pentanenitrile (99.5 %, Aldrich), pentanoyl chloride (> 97 %, Merck), hexylamine (99 %, Merck), dihexylamine (98 %), pentanamide (99 %, Acros), p-xylene (99+ %, Aldrich), triphenylphosphine (>99 %, Fluka), and 1,3-bis(diphenylphosphine)propane (97 %, Aldrich) were used without further purification. $RuCl_3{\cdot}3H_2O$ and $[RuCl_2(PPh_3)_3]$ were obtained from Strem Chemicals and used as received. $[RuCl_2(cod)]_x$,[30] $[RuH_2(PPh_3)_3]$,[31] and $[RuH_2(PPh_3)_4]$[32] were synthesized according to the literature procedures.

Standard procedure for the neat hydrolysis of pentanenitrile in the presence of hexylamine: The reaction mixture of pentanenitrile (8.6 mmol, 0.71 g), hexylamine (8.6 mmol, 0.87 g), water (17.2 mmol, 0.31 g), and $[RuH_2(PPh_3)_4]$ (0.5 mol %, 4.3 μmol, 49 mg) was first prepared in an inert atmosphere. At room temperature the homogeneous reaction mixture was charged into a 7-mL stainless-steel autoclave containing a glass insert. The autoclave was then heated to a set temperature, which was kept constant during the reaction. After the preset reaction time the reaction vessels were removed from the heating mantle and immersed in an ice/water bath to quench the reaction. The experiments were checked for leaks by weighing the autoclave before and after each reaction. After cooling, the reactors were opened and the content was removed and homogenized with ethanol, if necessary. Each reactor was rinsed twice with ethanol. The conversion and yield were determined with GC analysis by using p-xylene as an internal standard. To investigate the influence of the concentration on the course of the reaction, the initial concentrations of the various components were varied.

For the catalyst-free experiments at elevated temperature, the reaction mixture was biphasic at room temperature when 10 equivalents of water compared to the amount of nitrile were used. The phase behavior for these experiments is not known and therefore these data give only a qualitative insight into the global kinetics.

Hexylamine amidation experiments with pentanamide: The reaction between pentanamide, hexylamine, and water was used to study the amidation. The reaction mixture consisting of pentanamide (7.4 mmol, 0.75 g), hexylamine (7.4 mmol, 0.99 mL), and water (14.8 mmol, 0.27 mL) was first brought into a reactor insert in an inert atmosphere. The rest of the procedure was the same as for the hydrolysis experiments. For the hexylamine amidation with pentanamide under dry conditions, pentanamide was dried by using azeotropic toluene distillation. Hexylamine was dried by distillation over sodium hydroxide. The complete reactor was dried in an oven before use.

***N*-hexylpentanamide synthesis**: Pentanoyl chloride (0.51 mol, 61.2 g) was added dropwise to a solution of hexylamine (1.02 mol, 103 g) in diethyl ether (300 mL) and left overnight. The product mixture was distilled under vacuum, extracted with acidified water and brine, and dried over Na_2SO_4. A 97 % pure product was obtained and was used for product identification. Orange, red oil; 1H NMR (300 MHz, $CDCl_3$) $\delta = 6.30$–6.40 (s, 1H), 3.17 (t_d, $^3J_t = 7$ and $^3J_d = 6$ Hz, 2H), 2.14 ppm (t, $^3J = 7$ Hz); ^{13}C NMR (300 MHz, CDCl3) $\delta = 173.3$, 39.3, 36.2, 31.3, 29.4, 27.8, 26.4, 22.3, 22.2, 13.7, 13.6 ppm.

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