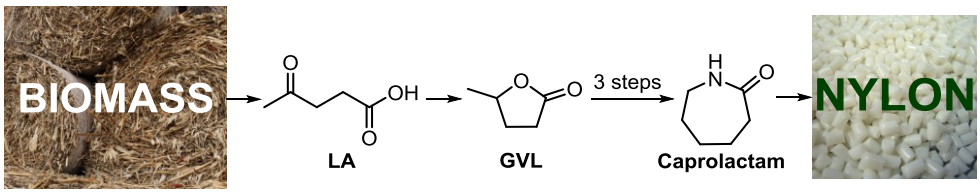
Development of homogeneous catalysts for the selective conversion of levulinic acid to caprolactam

Raoufmoghaddam, S.

5

From Renewable Feedstock to "Green" Nylon: Catalytic Conversion of γ-Valerolactone to ε-Caprolactam



This chapter has been submitted as a paper;
S. Raoufmoghaddam, M. T.M. Rood, F. K.W. Buijze, E. Drent, E. Bouwman, *Chem. Eur. J.* **2013** *submitted*.

Abstract

The conversion of γ-valerolactone (GVL) in three atom-efficient steps into the important polymer precursor ε-caprolactam is reported. GVL can be obtained from the renewable resource cellulose. The bio-based GVL can be converted to a mixture of isomeric methyl pentenoates (MP) via trans-esterification with methanol; subsequent aminolysis with ammonia leads to a mixture of pentenamides (PA). The resulting pentenamides are ultimately converted into ε-caprolactam via the rhodium-catalyzed intramolecular hydroamidomethylation reaction. The hydroamidomethylation reaction consists of an initial hydroformylation of the alkene moiety of PA and subsequent ring-closing reductive amidation of the resulting aldehyde with the amide functionality.

5.1. Introduction

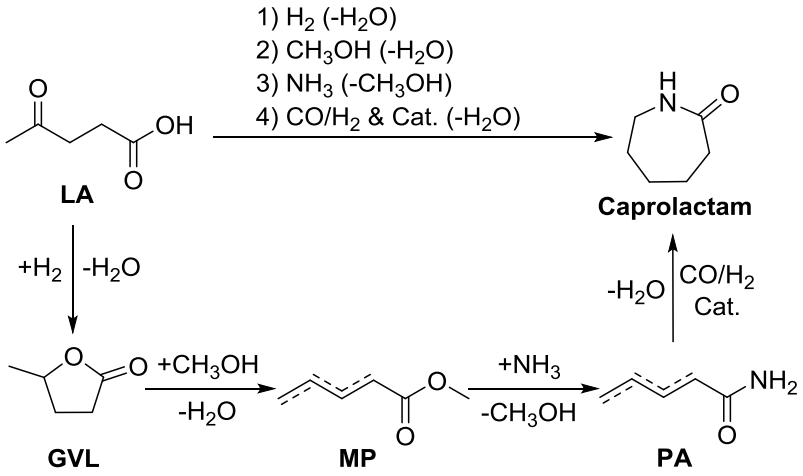
Societal concerns about climate change and long-term globally decreasing availability of fossil feedstock has stimulated chemical manufacturing industries to search for more sustainable routes to existing and new chemical products. In this respect developing alternative routes to large scale chemical products based on renewable biomass feedstock is a highly desirable goal of the chemical industry. Lignocellulosic biomass is one of the most attractive renewable feedstocks for production of bulk and fine chemicals, even more so when the novel synthesis routes from this feedstock allow for more atom and energy efficient production processes, producing less waste relative to the conventional routes.[1-3]

ε-Caprolactam is the polymer precursor for nylon-6, an extensively used synthetic polymer with an annual production of about four million tons.[4] It is traditionally synthesized from oil-based feedstock (benzene). The production of ε-caprolactam is typically carried out in a four step procedure[5] using benzene as the feedstock that is first hydrogenated to cyclohexane, which is subsequently converted to cyclohexanone by oxidation.[6, 7] The resulting cyclohexanone is then reacted with hydroxylamine to form cyclohexanone oxime,[8, 9] which is ultimately converted through a Beckmann rearrangement to ε-caprolactam.[10-12] The production of caprolactam by the traditional route suffers from a high energy demand, as well as co-production of large amounts of ammonium sulfate. The increasing demand for ε-caprolactam has provoked chemical companies to explore improvements in this classical synthesis route (e.g. Sumitomo process) as well as alternative production pathways, although most of these still rely on the use of fossil feedstock.[13-16]

An alternative route to produce caprolactam from renewable resources could be based on the use of levulinic acid, as this compound is foreseen to be readily available from cellulosic waste.[17, 18] Levulinic acid (LA) can be considered as a typical "functional platform chemical"[19] that can be converted into a range of derivatives widely usable in industrial applications,[20-22] e.g. to produce γ-valerolactone (GVL).[23-27] The conversion of LA into GVL by hydrogenation to 4-hydroxypentanoic acid using ruthenium catalysts, followed by (spontaneous) cyclization forming the lactone has been reported to occur in high efficiency (>95%).[28-30]

Herein, we report a novel synthesis route to caprolactam as depicted in Scheme 5.1, based on GVL as starting material; only water is generated as by-product of the

reactions. The first step of the proposed route proceeds via the acid-catalyzed reactive distillation of a mixture of isomeric methyl 2-, 3- and 4-pentenoates (MPs) from an acidic GVL/methanol mixture. In a subsequent reaction with ammonia this isomeric mixture of MPs is converted into the corresponding mixture of pentenamides (PAs). The selective conversion of the mixture of PAs to caprolactam is then carried out through a rhodium-catalyzed alkene isomerization- intramolecular hydroamidomethylation tandem reaction. An intermolecular version of the hydroamidomethylation reaction involving an alkene and amide as separate reactants is described in Chapter 3.



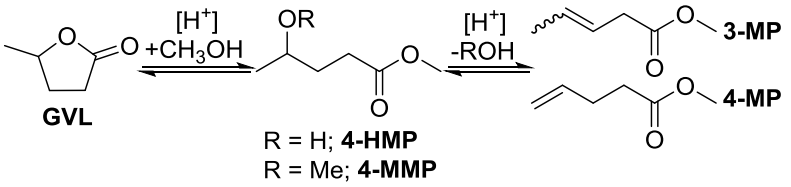
Scheme 5.1. Synthesis route for the conversion of levulinic acid to caprolactam

5.2. Result and discussion

5.2.1. Catalytic distillation of methyl pentenoates

Several patents describe the gas-phase synthesis of methyl pentenoates from GVL and methanol using solid acids as catalysts.[31, 32] Compared to the gas-phase reaction the catalytic distillation allows for relatively lower capital and energy costs as reaction and separation are combined in a single processing step with higher yield of the desired products because of the continuous removal of the methyl pentenoates formed in the reaction.[33, 34]

Trans-esterification of GVL with methanol was carried out via a reactive distillation using a strong Brønsted acid as the catalyst in the reaction mixture, following the procedure reported by Lange et al. (Scheme 5.2).[33, 34] Catalytic distillation takes the advantage of the large difference in boiling point between GVL and MPs (50 - 80 °C)[35] and drives the reaction to completion by continuously distilling the products from the equilibrium. In our study, the reported catalytic distillation was further optimized to lower reaction temperatures. During the reactive distillation process methanol must be continuously fed into the flask charged with GVL and the acid catalyst *p*-toluenesulfonic acid (HOTs). The distillate comprises a mixture of methanol, water, (cis & trans) methyl 3-pentenoates (3-MP) and methyl 4-pentenoate (4-MP) as well as small amounts of GVL, methyl 2-pentenoate (2-MP), methyl 4-methoxypentanoate (4-MMP) and methyl 4-hydroxypentanoate (4-HMP). After the reaction the residue in the bottom flask mainly consists of GVL, water and methanol, but also contains 4-MMP and 4-HMP as well as some heavy ends (see Appendix IV, Figure AIV.1 and AIV.2). Both the residual reaction mixture and the contents of the receiver flask were analyzed by GC and quantified by summation of the amounts in the distillate and bottom flask.[36]



Scheme 5.2. Reactive distillation of GVL in a stream of methanol results in a mixture of isomeric methyl pentenoates

A reaction temperature of 190 or 200 °C turned out to be the most beneficial for the conversion of GVL as well as the selectivity to MPs (Table 5.1). At these temperatures the selectivity to MPs is generally high, varying between 90-95%. Besides 3-MP and 4-MP, traces of 2-MP, 4-HMP and 4-MMP were also observed in the reaction mixture (see Appendix IV, Table IV.1). Neither dimethyl ether nor other by-products were detected, even upon placing the receiver in a liquid nitrogen trap, as similarly reported by Lange et al.[33, 34] At 190 °C the amount of intermediates was lower and a high conversion of GVL (>90%) was reached with good selectivity to MPs (95%). In the range of 150-200 °C, the reaction temperature does not have a considerable effect on

the 3-MP/4-MP ratio, which remains about 3. At temperatures higher than 200 °C the amount of GVL in the distillate increased and at temperatures lower than 150 °C the selectivity to MPs decreased. As reported, the use of higher alcohols like ethanol or butanol does not result in better selectivity to alkyl pentenoate esters compared to the results obtained with methanol.[33, 34, 37] The use of variable methanol feed rates revealed that 10 mL h^{-1} is an optimal rate; higher rates caused accumulation of GVL in the distillate and lower rates generally resulted in formation of more heavy ends.

Variation in the amount of HOTs from 1% to 10% showed that increasing the amount of HOTs increases the reaction rate and consequently decreases the reaction time (Entries 5, 7, 8). Furthermore, the use of a catalytic amount of H_2SO_4 as an alternative acid catalyst resulted in a slightly higher reaction rate (Entry 9).

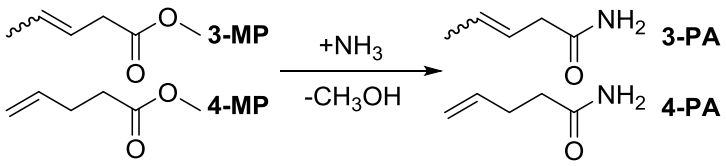
Table 5.1. Conversion of γ-valerolactone to methyl pentenoates via reactive distillation[a]

	T	conv. %	selectivity % [b]					
	°C	**GVL**	**2-MP**	**3-MP**	**4-MP**	**4-MMP**	**4-HMP**	**Other P**
1	150	40	0.2	61	24	9	1	5
2	160	54	0.2	61	26	7	0.7	4
3	170	62	0.2	66	25	5	0.5	4
4	180	63	0.2	66	23	6	0.5	4
5	190	90	0.1	73	23	2	0.2	2
6	200	91	0.2	70	22	3	0.2	5
7[c]	190	31	0.0	67	25	7	1	2
8[d]	190	56	0.2	67	23	4	1	4
9[e]	190	93	0.1	71	24	2	0	3

[a] Reaction conditions: 100 mmol (9.5 mL) GVL, 10 mmol (1.9 g) HOTs, 10 mL MeOH, T = 150 ºC – 200 ºC, t = 8 h, MeOH feed rate: 10 mL h^{-1}. The receiver flask was cooled with liquid N_2. [b] The selectivity was determined based on the amount of products in distillate and the bottom flask by GC analysis using decane as an external standard (for detailed information about the separate amounts in the distillate and the bottom flask, see Appendix IV); [c] 1 mmol HOTs; [d] 5 mmol HOTs; [e] 10 mmol (532 µL) H_2SO_4 as acid catalyst.

5.2.2. Conversion of methyl pentenoates to pentenamides

We have next investigated how the methanol solution of methyl pentenoates produced in the reactive distillation subsequently can be converted to the corresponding pentenamides (PA) (as depicted in Scheme 5.3) using various sources of ammonia, including ammonia gas, aqueous ammonia (35%) and methanolic ammonia (7 N).[38]



Scheme 5.3. Conversion of methyl pentenoates (MP) to pentenamides (PA)

Direct reaction of the methanolic distillate containing the methyl pentenoate mixture with (methanolic or aqueous) ammonia gave only low conversion to pentenamides, as expected. The reaction of the methyl esters with ammonia is an equilibrium reaction and the presence of excess of methanol pushes the equilibrium to the esters. Therefore methanol was distilled from the mixture prior to the addition of different sources of ammonia (Table 5.2). The application of 8 bar ammonia gas resulted in nearly full conversion, but the reaction was slow and needed more than 20 h residence time (Entry 1). It appeared that the use of aqueous ammonia (35%) gave the best results: a reaction at 80 °C after only 6 h resulted in >98% yield of combined PAs (Table 5.2, entry 4). Generally, 4-MP was converted more slowly than 3-MP which can be rationalized by the different inductive electron-withdrawing effect of the alkene double bond in the respective isomers. Surprisingly, pentenoic acids or ammonium pentenoates were not formed under these conditions.

Table 5.2. Results of the aminolysis of a mixture of methyl pentenoates to pentenamides (PA) using different sources of ammonia[a]

	NH_3 source	NH_3 amount	t h	conversion %	yield %[b] **3-PA**	**4-PA**
1	7N NH_3 in MeOH	50 mmol	5	13		
2	NH_3 (g)	8 bar	20	96	99	80
3	NH_4OH (35%)	50 mmol	5	93	96	80
4	NH_4OH (35%)	50 mmol	6	99	99	96

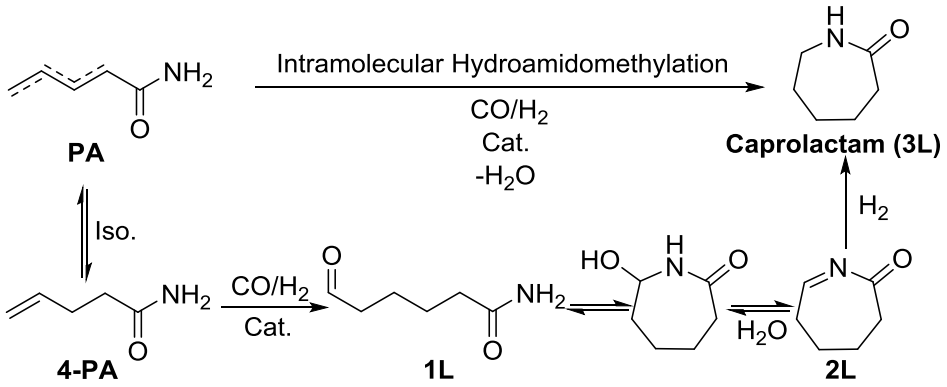
[a] Reaction conditions: 10 mmol (1.14 g) of methyl pentenoates (3-MP (7.5mmol)/4-MP (2.5mmol)); T= 80 °C; t= 5-20 h; [b] The yield was determined by GC analysis using decane as an internal standard; The amounts of the mixture of methyl pentenoates determined by injecting the mixture into GC before starting the reaction (for detailed information see Appendix IV, Table AIV.2)

Alkene double bond isomerization was also not observed, as the ratio of produced 3-PA and 4-PA was equal to the starting 3-MP/4-MP ratio at 99% overall MP conversion (Entry 4). To further study any possible occurrence of base-catalyzed isomerization, pure 4-MP was separately reacted under the same conditions; only 4-PA was formed and no other isomers were observed (see Appendix IV, Table AIV.2).

5.2.3. Intramolecular hydroamidomethylation of pentenamides to caprolactam

The regioselective intramolecular hydroamidomethylation of the resulting mixture of pentenamides (PA) is a novel and the most challenging step of the newly designed route to obtain caprolactam from levulinic acid. Inspired by our recent achievements concerning the catalytic hydroamidomethylation of alkenes (Chapter 3) and reductive amidation of aldehydes (Chapter 2) we have thus investigated the rhodium-catalyzed intramolecular hydroamidomethylation of pentenamides, a reaction that consists of an initial isomerization step (for internal pentenamides), followed by hydroformylation and a subsequent intramolecular reductive amidation reaction (Scheme 5.4).

We started our investigations of this intramolecular hydroamidomethylation reaction using pure 4-PA as the substrate under catalytic conditions as developed for the reductive amidation of an aldehyde. The use of an Rh/xanthphos catalyst system in the presence of an acid co-catalyst in a syngas atmosphere resulted in only very low yields of caprolactam (~4%; Table 5.3, entry 1).



Scheme 5.4. Intramolecular hydroamidomethylation of pentenamide to caprolactam (For clarity only the linear products are depicted)

The main product appeared to be (unsaturated) polymeric material as deduced from the insoluble white product that was formed. Soluble by-products observed in GC-MS appeared to be unsaturated dimer (m/z=240) and its hydrated derivative (m/z=258) as well as some other unidentified compounds; the higher molecular mass products could not be identified using GC-MS. It appeared that the unsaturated caprolactam (**2L**) was the major other reaction product with a total selectivity of about 40%. Only a very low amount of branched 6-ring unsaturated lactam **2B** was formed. Additionally, some 15% of hydrogenated substrate, pentanamide (valeramide, VA) was obtained. Surprisingly, this catalytic system is unable to hydrogenate the unsaturated caprolactam product, but prone to hydrogenate the unsaturated pentenamide. As we have found that the hydrogenation activity of the rhodium catalyst in the catalytic hydroamidomethylation of alkenes with acetamide is strongly promoted by the presence of 1,1,1,3,3,3-hexafluoro-isopropyl alcohol (HOR^F), we applied HOR^F as a co-additive in the reaction of 4-PA. As shown in entry 2, selective intramolecular hydroamidomethylation of 4-PA could still not be accomplished; the unsaturated lactam **2L** was the major product. Surprisingly, when the strong acid HOTs was omitted from the catalyst system, a high yield of **2L** was obtained (entry 3), and even 10% of caprolactam was formed. A very significant decrease in oligomeric material was observed, indicating that the presence of acid merely leads to (cationic) polymerization of the unsaturated lactam **2L**. A further increase of the amount of HOR^F to solvent-like quantities in the absence of HOTs resulted in a significant increase in the selectivity to caprolactam **3L** up to about 25% (Entry 4). This increase is associated with a decrease in unsaturated lactams, thus showing the promoting effect of HOR^F on the hydrogenation activity of this catalytic system in a syngas environment. Unfortunately, a significant amount of valeramide (VA) was still co-produced, which is increasing with HOR^F and HOTs concentration (Entry 5).

In our next attempts we aimed at the formation of 6-oxohexanamide **1L** by hydroformylation of 4-PA, with the intention to carry out the ring-closing reductive amidation in a separate subsequent step. Attempted hydroformylation of 4-PA with an Rh system in the absence of any phosphane ligand or in the presence of monodentate phosphane ligands in the absence of both HOR^F and HOTs gave high conversions and surprisingly showed the formation of both unsaturated cyclic products **2** with combined chemoselectivities up to about 90%. However, a modest ratio of 7- over 6-membered cyclic unsaturated products (**2L**/**2B**) was obtained, indicating a relatively low

regioselectivity for linear aldehyde formation in the hydroformylation of 4-PA (See Appendix IV, Table AIV.3).

The performance of *in situ* formed Rh catalysts in the 'hydroformylation' of 4-PA with a number of xantphos-type ligands (Figure 5.1) is shown in entries 6-9. Remarkably, good conversions (60-98%) and chemoselectivities up to 90% for the unsaturated intermediates **2** were generally obtained at 100 ºC. A very high preference (~up to 99%) for 7-membered cyclic unsaturated product **2L** versus 6-membered **2B** was observed. Additionally, small amounts of caprolactam **3L** as well as even smaller amounts of oligomer/polymer and VA were formed under these conditions (see Appendix IV, Table AIV.3).

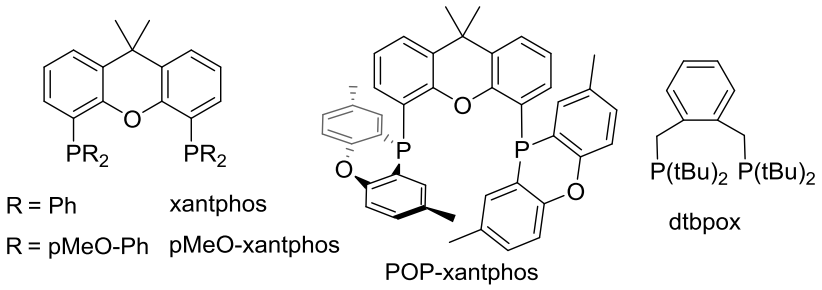
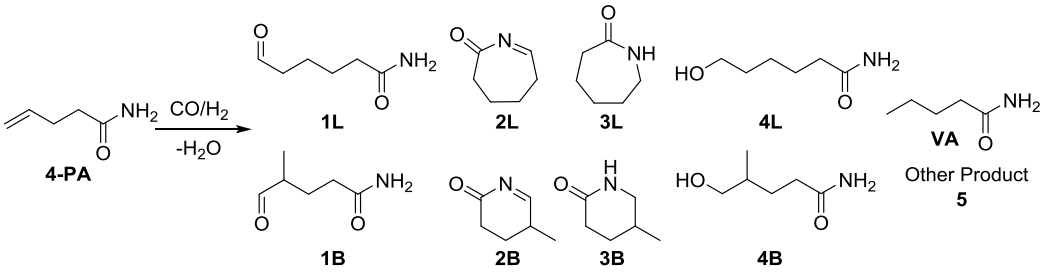


Figure 5.1. Selected ligands used in the intramolecular hydroamidomethylation of pentenamides (PA)

Apparently, the aldehyde functionality formed in the hydroformylation reaction immediately cyclizes with the amide functionality while extruding H_2O to form the unsaturated lactam **2L**. It is imperative to note that the 7-membered cyclic product is by far dominant over the 6-membered cyclic product in all experiments with xantphos-type ligands (~98%). The use of another bidentate phosphane ligand, such as dtbpox, -well-known for inducing a similarly high linear regiochemistry in palladium-catalyzed carbonylation[39] -gave not only lower catalytic activity, but also a low ratio of **2L**/**2B** indicating low regioselectivity for the linear aldehyde in hydroformylation (Entry 9). This clearly is a consequence of the ability of Rh/xantphos hydroformylation catalyst systems to impose a very high regioselectivity for the formation of the linear aldehydes from higher paraffinic alkenes.[40] Of the ligands tested the POP-xantphos ligand is the most interesting, as significant alkene bond isomerization (6% from 4-PA mainly to 3-

PA) took place under the applied reaction conditions (Entry 8). In all instants the selectivity to caprolactam was only about 10% (Entry 10).

Table 5.3. Influence of various conditions on intramolecular hydroamidomethylation of 4-PA[a]



	Ligand	t	T	P (CO/H_2)	HOTs	HOR^F	conv.	selectivity % [b]						L[c]
		h	°C	bar	mmol	mmol	%	**VA**	**1**	**2**	**3**	**4**	**5**	%
1	xantphos	8	100	50(1/2)	0.025		80	14	1	38	4	0	43	97
2	xantphos	8	100	50(1/2)	0.025	5	90	18	1	46	5	0	31	98
3	xantphos	8	100	50(1/2)		5	84	10	2	77	10	0	2	99
4	xantphos	8	100	50(1/2)		20	95	15	5	53	24	0	3	99
5	xantphos	8	100	50(1/2)	0.025	20	95	22	1	28	24	0	26	98
6	xantphos	8	100	50(1/2)			81	1	1	88	7	0	3	99
7	pMeO-xantphos	8	100	50(1/2)			62	0	2	90	2	0	6	98
8	POP-xantphos	8	100	50(1/2)			85	2	1	82	3	0	12[e]	94
9	dtbpox	8	100	50(1/2)			100	1	0	92	0	0	7	61
10	xantphos	10	100	50(1/2)			98	1	1	84	10	0	4	99
11[d]	xantphos	8+4	100-80	50(1/2)-80 H_2			100	15	1	5	68	0	12	99
12[d]	pMeO-xantphos	8+4	100-80	50(1/2)-80 H_2			91	23	1	24	46	0	7	98
13[d]	POP-xantphos	8+4	100-80	50(1/2)-80 H_2			100	20	0	11	57	0	13	96
14[d]	xantphos	10+4	100-80	50(1/2)-80 H_2			100	3	1	12	78	0	6	99
15[d]	xantphos	10+6	100-80	50(1/2)-80 H_2			100	3	1	2	88	0	6	99

[a] Reaction conditions: 2 mmol (19.8 mg) of 4-PA; 0.0025 mmol (1.24 mg) $[Rh(cod)Cl]_2$; 0.02 monodentate or 0.01 mmol bidentate ligand; $P(CO/H_2)$ = 50(1/2) bar; T = 100 °C; *t* = 8-10 h; 0-0.025 mmol HOTs; 0-20 mmol HOR^F; Solvent: 10 mL diglyme. [b] The amounts of products were determined by GC analysis using undecane as an internal standard; [c] overall linearity of the reaction mixture determined by GC; [d] In a one-pot two stage operation; reaction conditions: 8-10 h at 100 °C hydroformylation-depressurizing syngas-flushing with H_2- pressurizing with 80 bar H_2- 4-6 h at 80 °C hydrogenation

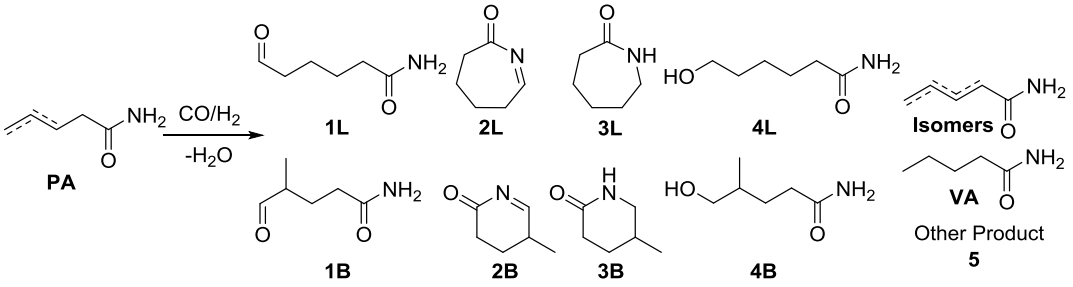
Hydroformylation of 4-PA by Rh/PPh_3 catalytic systems in THF has been reported before.[41, 42] Remarkably, it has been reported that the use of several rhodium precursors in the presence of PPh_3 resulted in >80% yield of the branched 6-membered cyclic unsaturated lactam, which was explained by the regioselectivity being driven by amide-directed "chelation control".[41] We have repeated the experiment in THF using [$RhHCO(PPh_3)_3$] as described by Ojima et al;[42] in our hands this indeed resulted in the formation of mainly product **2**, however, with a **2L**/**2B** ratio of ~0.8, similar to our reactions in diglyme (see Appendix IV, Table AIV.4).

To overcome the sluggishly proceeding hydrogenation of the unsaturated cyclic hydroformylation products under syngas conditions we attempted a two-step protocol in which Rh/xantphos was used as the single catalyst system. After the hydroformylation and subsequent cyclization stage syngas was replaced with pure dihydrogen gas and the mixture was further reacted at 80 ºC in a second stage of the reaction (Table 5.3, Entries 11-15). It was gratifying to observe in our best experiments an overall ~90% yield for caprolactam **3L** based on 4-PA as the feed, while only relatively small amounts of by-products were formed (Table 5.3, Entry 15).

Finally, as the ultimate challenge we studied the hydroamidomethylation reaction starting with an internal alkene, at first employing pure 3-pentenamide (Table 5.4, entries 1-7). Hydroformylation of 3-PA with the Rh/xantphos system under a pressure of 50 bar syngas gave only low conversion after 8 h; the main products observed were VA and **2** in addition to other products **5**, with a low **2L**/**2B** ratio (Entry 1). Using a lower pressure of 10 bar syngas resulted in a slightly higher conversion and higher selectivity for lactam **2** with a **2L**/**2B** ratio of 1. POP-xantphos is known to be a relatively good ligand for catalyzing the isomerization-hydroformylation tandem reaction of simple paraffinic alkenes yielding linear aldehydes when using lower syngas pressure (10 bar) and higher temperature (120 °C).[43-46] Application of this ligand at 100 or 120 °C in the hydroformylation of 3-PA resulted in ~50% selectivity to the unsaturated lactams **2** of which about 60-65% is the unsaturated 7-membered ring **2L** (Entries 3, 4). At 120 ºC good conversion is reached, however, a larger amount of valeramide (VA) is formed which can be explained by chelate formation of the Rh-sec-alkylamide (see below). Application of an even lower pressure of 5 bar syngas does not further improve these results (Entry 9), whereas at a higher reaction temperature of 130 °C the selectivity for **2** goes down in favor of the production of VA (Entry 6).

The use of a 1:1 mixture of 3-PA and 4-PA using the standard Rh/xantphos system resulted in approximately 50% conversion with ~70% selectivity to **2L**; however, it is clear that mainly reaction of 4-PA occurs (Entry 8). Application of the POP-xantphos system at lower pressure and higher temperature resulted in 80% conversion, the main product being **2** with 77% **2L** (Entry 9). Finally, using a mixture of pentenamides produced from GVL as the substrate gave ~80% conversion and revealed approximately 60% selectivity to **2** with ~75% overall selectivity for linear products (Entry 10, for more information Appendix IV, Table AIV.7).[47]

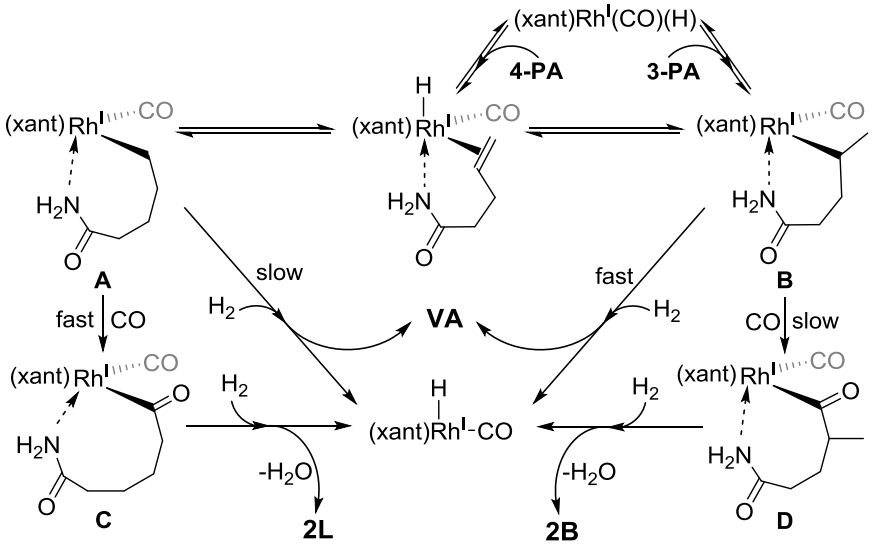
Table 5.4. Influence of various conditions on intramolecular hydroamidomethylation of pentenamides (PA)[a]



	substrate	Ligand	t	T	P(CO/H$_2$)	conv.	selectivity % [b]						L[d]
			h	°C	bar	%	**VA**	**Iso**[c]	**1**	**2**	**3**	**4**	**5**	%
1	3-PA	xantphos	8	100	50(1/2)	16	39	3	3	35	0	0	19	42
2	3-PA	xantphos	8	100	10(1/1)	19	18	3	0	53	0	0	26	48
3	3-PA	POP-xantphos	8	100	10(1/1)	20	20	17	0	47	1	0	15	59
4	3-PA	POP-xantphos	8	120	10(1/1)	86	32	2	2	53	2	0	9	66
5	3-PA	POP-xantphos	16	120	10(1/1)	100	34	2	2	51	1	0	11	65
6	3-PA	POP-xantphos	8	120	5(1/1)	82	29	6	2	54	0	0	9	63
7	3-PA	POP-xantphos	8	130	10(1/1)	92	42	2	2	42	0	0	12	68
8[e]	3-PA&4-PA	xantphos	8	100	50(1/2)	52	15	0	5	72	4	0	4	95
9[e]	3-PA&4-PA	POP-xantphos	8	120	10(1/1)	81	29	1	2	60	1	0	8	77
10[f	3-PA&4-PA	POP-xantphos	8	120	10(1/1)	83	31	0	2	58	2	0	8	73

[a] Reaction conditions: 2 mmol (19.8 mg) of 3-PA or 4-PA; 0.0025 mmol (1.24 mg) [Rh(cod)Cl]$_2$; 0.01 mmol ligand; P(CO/H$_2$)= 5-50(1/1-1/2) bar; T=100-130 °C; t=8-16 h; Solvent: 10 mL diglyme; [b] The amount of products was determined by GC analysis using undecane as an internal standard; [c] mixture of pentenamide isomers (containing minor amounts of 2-PA, 4-PA); [d] overall linearity of **1**, **2**, **3** & **4** determined by GC; [e] 3-PA and 4-PA (1 mmol each). [f] The mixture of 3-PA (1.5 mmol) and 4-PA (0.5 mmol) produced from GVL; the amounts of pentenamides was determined by injecting the mixture into GC before starting the reaction

It thus appears that the most challenging step in our synthetic route is the intramolecular hydroamidomethylation reaction starting from the mixture of pentenamides. Starting from 4-PA and using the xantphos/Rh catalytic system under 'hydroformylation' conditions results in the formation of the 7-membered unsaturated lactam **2L** in high yields. The use of rhodium systems without ligands or with ligands that do not induce high regioselectivity in hydroformylation of alkenes resulted in the formation of the 6-membered product **2B** as reported earlier,[41, 42] as well as **2L**, but also resulted in the hydrogenation of the substrate to valeramide (VA). Similarly, the use of 3-PA as a substrate resulted in a mixture of **2L** and **2B**, but with the formation of even larger amounts of VA. The formation of VA in the hydroamidomethylation reaction of pentenamides may be explained by the chelating nature of the pentenamide substrate.

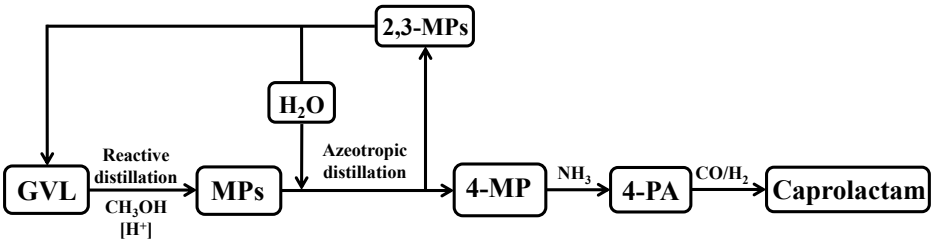


Scheme 5.5. Proposed mechanistic pathways toward the formation of various products

As depicted in scheme 5.5, coordination of 4-PA to a rhodium-hydride catalyst followed by hydride migration may either give the primary Rh-alkyl species **A** or the secondary Rh-alkyl species **B**. Both species may be further stabilized by the coordination of the amide group thus forming a 7-membered or 6-membered chelate ring, respectively.

Reaction of 3-PA with the Rh-hydride will also result in species **B** but possibly also the other isomeric secondary Rh-alkyl species; the latter may be less likely due to the more strained 5-membered chelate ring, which is in agreement with the fact that the 5-membered lactam product was not observed in our reactions. Migratory insertion of the primary Rh-alkylamide structure **A** to CO will give Rh-acyl species **C**, subsequent hydrogenolysis results in the formation of the linear aldehyde, which cyclizes to **2L**. Migratory insertion of the Rh-sec-alkyl-amide structure **B** to CO to form Rh-acyl species **D** may be disfavored for steric reasons and relatively strong chelation of the amide functionality, the hydrogenolysis rate of the Rh-alkyl species **B** may be promoted due to the relatively strong chelation of the amide functionality, resulting in the formation of VA.

Hence, the limiting factor that needs further research is the development of a catalyst that is able to isomerize rapidly the internal alkenes 2-PA and 3-PA to the terminal alkene 4-PA prior to hydroformylation, before hydrogenolysis of the secondary Rh-alkyl species occurs, which leads to the formation of VA.



Scheme 5.6. A Schematic outlook for the formation of caprolactam

It has been reported that GVL can be converted into 4-MP with higher selectivity (60%) using basic heterogeneous catalysts ($CsOAc/SiO_2$) at a very high temperature (350 °C),[48] but even if an efficient tandem hydroformylation-reductive amidation catalytic system with the desired additional attributes of i) high alkene isomerization-hydroformylation activity and ii) at the same time inhibiting hydrogenation of in particular the 2- and 3-PA isomers cannot be achieved, it may still be attractive to use the present Rh/xantphos catalyst system allowing close to 90% selective conversion of 4-PA only to caprolactam. In such instance isomerization/separation techniques to separate 4-MP from the mixture of 2-, 3- and 4-MPs generated via reactive distillation

by selective azeotropic distillation of 4-MP[49] with continuous recycle of the other isomers to the reactive distillation section can be advantageously undertaken (Scheme 5.6).

In conclusion, we have proposed and developed a novel reaction scheme for the atom-economic conversion of γ-valerolactone into the important polymer precursor ε-caprolactam. GVL, which may be prepared from bio-based levulinic acid, can be converted in two steps with high yields into a mixture of pentenamides via reactive distillation of GVL to methyl pentenoates and subsequent aminolysis using aqueous ammonia.

5.3. Experimental

5.3.1. General

The stainless steel autoclave reactors (100 ml) were of HEL Limited, UK, equipped with magnetic stirrer, pressure transducer and temperature controlling thermocouple. A Hewlett Packard HP6890 Series auto-sampler GC system was used for regular GC analysis. GC-MS analysis were carried out on an Agilent technologies 7820A GC system series coupled with an Agilent technologies 5975 series GC-MSD system. A glovebox of M. Braun Inert gas-System GmbH, Germany, was used for storing and handling of air-sensitive phosphane ligands. Nuclear magnetic resonance spectra were recorded on a Bruker DPX300 (300MHz) or a Bruker DMX400 (400MHz) spectrometer. A Syringe Pump NE1000 series auto-injector from ProSense B. V. (laboratory and process Equipment Company) was used for the reactive distillation pumping methanol continuously into the reaction mixture. Innovative Technologies PureSolv MD 5 Solvent Purification System was used for drying solvents. All reaction preparations and manipulations were performed using standard Schlenk techniques under an argon atmosphere. The catalytic reactions were carried out under varying syngas pressures and reaction temperatures.

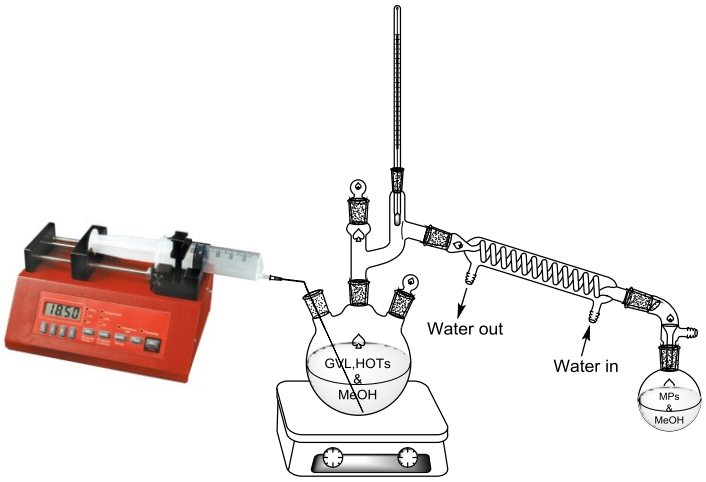
5.3.2. Chemicals

The solvent bis(2-methoxyethyl)ether (diglyme) was distilled from CaH_2, deoxygenated and used immediately after the purification process. All other solvents were purged with argon and purified under pressure of dry argon using an Innovative Technologies purification system. The solvents passed through activated columns under low pressure to remove trace impurities. Stainless Steel Schlenk Vacuum line and Sigma Aldrich Air-free flasks allow them to be safely transferred.

3-Pentenoic acid, 4-pentenoic acid, methy-3-pentenoate, gamma valerolactone, valeramide, caprolactam, methanolic ammonia (7N), ammonia gas cylinder, aqueous ammonia (35%), decane (internal standard), undecane (internal standard), para-toluenesulfonic acid (HOTs), trifluoromethanesulfonic acid (HOTf), sulfuric acid, bis(2-methoxyethyl) ether (diglyme), 1,1,1,3,3,3-hexafluoroisopropyl alcohol (HOR^F) methanol, ethanol and other solvents, acids and bases were purchased from Acros Organics and Sigma Aldrich, the Netherlands and used as received. The rhodium precursors (acetylacetonato)dicarbonylrhodium(I), chlorido(1,5-cyclooctadiene)rhodium(I) dimer, bis(1,5-cyclooctadiene)rhodium(I) trifluoromethanesulfonate, were purchased from Acros Organics and Sigma Aldrich, the Netherlands and used as received. The phosphane ligands triphenylphosphane (PPh_3), Tris(2,4-ditert-butylphenyl)phosphite ($P(O\text{-}di\text{-}tBu\text{-}Ph)_3$), 9,9-dimethyl-4,5-bis(diphenyl-phosphanyl)xanthene (xantphos), xantamidite and xantphite were purchased from Strem Chemicals, Germany and Sigma Aldrich, the Netherlands and used as received. The bidentate phosphane ligands benzoxantphos, and POP-xantphos were purchased from Innovative Catalyst Technologies (InCatT B.V.), The Netherlands and used as received. The phosphane ligands tetraphos, Bryant-5 and naphthol-3 were generously provided by DSM, The Netherlands and used as received. The other phosphane ligands such as diphenyl(2-pyridyl)phosphane (PPh_2Py), bis(di-tert-butylphosphino)-o-xylene (dtbpox), 2,7-di-tert-butyl-9,9-dimethyl-4,5-bis(diphenylphosphanyl)xanthene (tBu-xantphos), 4,6-bis(diphenylphosphanyl)-10,10-dimethyl-10H-dibenzo[b,e][1,4]oxasilane (Si-xantphos), 9,9-dimethyl-4,5-bis(di-orthomethoxyphenyl-phosphanyl)xanthene (oMeO-xantphos), 9,9-dimethyl-4,5-bis(di-paramethoxyphenyl-phosphanyl)xanthene (pMeO-xantphos) and 4,5-bis(di(tert-butyl)phosphanyl)-9,9-dimethylxanthene ($xantphos(tBu)_2$) were generously provided by Shell Global Solutions Amsterdam b.v., The Netherlands and used as received.

5.3.3. Catalytic Reactive Distillation of methyl pentenoates

The reaction was performed in a 100 mL three-necked round bottom flask loaded with GVL (9.5 mL, 100 mmol) and acid catalyst (1 – 10 mmol) were dissolved in 10 mL of MeOH. The flask was connected to a micro distillation device which was connected to a 100 mL round bottom flask used as a receiver. The receiver flask was cooled down with liquid N_2. The solution was heated to a set temperature, 150 °C- 200 °C for 4-8 h. During this time MeOH was added to the bottom of the reactor flask at a rate of 10 mL/h. After a specified time, the contents of both the reactor flask and the receiver were analyzed by GC adding decane (2.5 mmol, 0.487 mL; 250 mM in 10 mL volumetric flask) as an external standard.



The reactor flask generally yielded a yellowish clear solution that contained a mixture of unreacted gamma valerolactone (GVL), methyl 4-hydroxypentenoate (4-HMP) and methyl 4-methoxypentenoate (4-MMP) intermediates, methyl 2-pentenoate (2-MP), methyl 3-pentenoate (3-MP), methyl 4-pentenoate (4-MP), and methyl para-toluenesulfonate. The receiver flask contained a clear colorless solution that was found to be a mixture of MeOH, water, 4-MP, 3-MP followed by traces of 2-MP and GVL.

5.3.4. Aminolysis of methyl pentenoates to pentenamides

5.3.4.1. In methanolic ammonia

The reaction was carried out in a 50 mL round bottom flask loaded with 5 mL of a methyl pentenoates solution in MeOH (0.9 M, a distillate from a reactive distillation experiment, concentration determined through GC calibration lines, 4.5 mmol total MP, (in approximate 3:1 ratio of 3-MP:4-MP, with traces of GVL; thus containing ~3.4 mmol 3-MP and ~1.1 mmol 4-MP) or methyl pentenoates (10 mmol, 1.14 g, ~3:1 ratio of 3-MP:4-MP, after evaporation of MeOH), NH_3 (7N) in MeOH (5 or 10 equivalent) and (1.2 mmol, 0.254 mL) undecane as an internal standard were mixed and stirred for different times at various temperatures between RT to 100 °C. After the experiment, the reaction mixture was taken and at once analyzed by gas chromatography. Calibration lines for each analyte were used in determining the yields of the various products. The assignments of the products were confirmed with GC-MS and comparison with authentic and pure commercial samples.

5.3.4.2. With ammonia gas

The reaction was carried out in a 300 mL autoclave reactor loaded with methyl pentenoates (MP) (10 mmol, 1.14 g) (after evaporation of MeOH) and (1.2 mmol, 0.254 mL) undecane as an internal standard. The autoclave was then tightly closed and subsequently filled with 6 bar of NH_3 (g) (~75 mmol) and stirred for different time and various temperatures between RT to 80 °C. After the experiment, 5 ml of dried and degassed solvent (diglyme or methanol) was added to the reaction mixture and this was then analyzed by gas chromatography. Calibration lines for each analyte were used in determining the yields of the various products. The assignments of the products were confirmed with GC-MS and comparison with authentic and pure commercial samples.

5.3.4.3. In aqueous ammonia (35%)

The reaction was carried out in a 50 mL round bottom flask loaded with methyl pentenoates (10 mmol, 1.14 g) (after evaporation of MeOH), aqueous ammonia 35% (50 mmol, 2.42 mL) and (1.2 mmol, 0.254 mL) undecane as an internal standard were mixed and stirred for 5-6 hours at various temperature between RT to 100 °C. After experiment, the reaction mixture was taken and at once analyzed by gas chromatography. Calibration lines for each analyte were used in determining the yields of the various products. The assignments of the products were confirmed with GC-MS and comparison with authentic and pure commercial samples.

5.3.5. Catalytic high pressure reaction

5.3.5.1. Catalytic intramolecualr hydroamidomethylation of pentenamides

For all the catalytic experiments the active catalyst precursor was formed by in-situ in the autoclave by transferring the 0.005 mmol of rhodium precursor as a metal and the 0.01 mmol of selected bidentate phosphane ligand or 0.02 mmol of selected mono-dentate phosphane ligand. In the preparation of the catalytic reaction mixture a rhodium precursors $[Rh(cod)Cl]_2$ (0.0025 mmol, 1.24 mg) and phosphane ligand for instance xantphos (0.01 mmol, 5.79 mg) were weighed and transferred into an autoclave. Next, the substrates 3-pentenamide or 4-pentenamide or mixture of pentenamides (2 mmol, 198 mg) were weighed and transferred into an autoclave. The autoclave was tightly closed and subsequently filled with argon with use of a Schlenk line that was connected to one of the valves of the autoclave. Through another valve under a continuous flow of argon subsequently was added 10 mL of dried and degassed solvent diglyme (or in some cases 8 mL of dried and degassed diglyme, 2 mL of HOR^F) and (1.2 mmol, 0.254 mL) undecane as an internal standard (and in some cases followed by 0.05 mmol (9.51 mg) or 0.025 mmol

(4.76 mg) HOTs). Then the reactor was inserted into the heating block and pressurized with 50 bar (CO/H_2=1/2) syngas. This reaction mixture was stirred at 500 rpm for 30 min to ensure that complex formation was complete. The reaction mixture was heated up to 100 °C (within 30 min) under stirring at 500 rpm. All reaction conditions of the catalytic process were controlled by computerized software panels. After standing for eight hours at this temperature, the autoclave was cooled down to room temperature over about one hour. The autoclave was then slowly vented to atmospheric pressure.

In a semi-one-pot reaction after depressurizing syngas and flushing with di-hydrogen gas, the reactor was pressurized with 50 - 100 bar di-hydrogen gas and then the reaction mixture heated up to 50 - 100 °C under stirring at 500 rpm for hydrogenation step. After standing for four - six hours at this temperature, the autoclave was cooled down to room temperature and then slowly vented to atmospheric pressure. After each catalytic run the reaction mixture was taken from the reactor and at once analyzed by gas chromatography. Calibration lines for each analyte were used in determining the conversion of the substrates and yields of the various products. The assignments of the products were confirmed with GC-MS and comparison with authentic and pure commercial samples.

5.3.6. Synthesis of Intermediates

5.3.6.1. Synthesis of 3-pentenamide[50-54]

Following the reported procedure, thionyl chloride (8.7 ml, 120 mmol) was added drop wise to *trans*-3-pentenoic acid (10 ml, 100 mmol) at 0 °C and the mixture was stirred at RT for 10 min and at 60 °C for 30 min. The excess thionyl chloride was evaporated and the oil was dissolved in 20 ml CH_2Cl_2. This solution was added drop wise to a solution of 7 N NH_3 in MeOH (150 ml, 1.0 mol) at 0 °C and stirred for 10 minutes at room temperature. The solvents were evaporated. Water (50 ml) was added and was extracted 2 times with 50 ml CH_2Cl_2. The combined organic layers were washed with 50 ml brine, dried over $MgSO_4$ and the solvents were removed *in vacuo* to give a white powder. Yield 7.93 g, 80%. ^{1}H-NMR ($CDCl_3$): δ = 6.65 and 5.99 (br s, 2x 1H, NH_2), 5.70-5.49 (m, 2H, 2 x CH), 2.96 (d, 2H, CH_2), 1.70 (m, 3H, CH_3). ^{13}C-NMR ($CDCl_3$): δ = 175.2 ($CONH_2$), 130.8 and 123.5 (2 x CH), 39.8 (CH_2), 17.9 (CH_3).

5.3.6.2. Synthesis of 4-pentenamide

The synthesis of 4-pentenamide was performed in a similar fashion as in 3-pentenamide starting from 4-pentenoic acid (15 ml, 150 mmol), thionyl chloride (13 ml, 180 mmol) and 200 ml 7 N NH_3 solution in MeOH. The yield was 13.6 g of a white powder (92%). ^{1}H-NMR ($CDCl_3$): δ = 5.91-5.78 (m, 1H, CH), 6.0 and 5.7 (br s, 2 x 1H, NH_2), 5.13-5.02 (m,

2H, CH_2=CH), 2.44-2.30 (m, 4H, 2 x CH_2). ^{13}C-NMR ($CDCl_3$): δ = 175.6 ($CONH_2$), 136.9 (CH), 115.7 (CH_2=CH), 35.1 and 29.4 (2 x CH_2).

5.3.6.3. Synthesis of methyl 4-methoxypentenoate

According to a literature procedure,[55] GVL (4.8 mL, 50 mmol) and trimethyl orthoformate (8.2 mL, 75 mmol) were dissolved in 50 ml of MeOH. 0.1 mL of sulfuric acid was added and the mixture was stirred at 50 °C for 3 h and stirred overnight at room temperature. Trimethyl orthoformate (1 mL, 10 mmol) was added and the solution heated to 50 °C for 6.5 h. The solvents were removed in vacuo and a saturated $NaHCO_3$ solution was added. The solution was extracted with ethyl acetate. The combined organic layers were dried with $MgSO_4$, then filtered and the solvents were removed. ^{1}H NMR (300 MHz $CDCl_3$, 25 °C, TMS): δ 3.7 ppm (s, 3H; $OCOCH_3$), 3.4 ppm (q, 1H; CH), 3.3 ppm (s, 3H; $CHOCH_3$), 2.4 ppm (t, 2H; CH_2CO), 1.8 ppm (q, 2H; $CHCH_2$), 1.2 ppm (d, 3H; CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ 76.0 ppm(CH), 56.1 ppm (CH_3OCO), 51.6 ppm (CH_3OCH), 31.3 ppm (CH_2CH), 30.0 (CH_2CO), 18.9 ppm (CH_3).

5.3.7. GC and GC-MS analysis

A GC trace of typical **reactive distillation of methyl pentenoates** (MP) is shown in the Appendix IV, Figure AIV.1 and AIV.2 with the assignment of products. 1 µL Crude reaction mixture containing external standard (decane; 2.5 mmol, 0.487 mL; 250 mM in 10 mL volumetric flask) was injected into a Hewlett Packard HP6890 Series auto-sampler GC system with column HP-1MS UI (30m*0.250mm*1.00µm). All the solvents have been assigned by comparing to their standard GC spectra. All the retention values of substrate and product to decane have been determined using commercially available or isolated standard chemicals. More detailed information about heavy-ends is shown in Appendix IV.

Analysis conditions: 130 ºC (5 min), ramp 50 ºC / min to 300 ºC, 300 ºC (3.6 min) (12 min in total).

A GC trace of typical **aminolysis of methyl pentenoates** (MP) to pentenamides (PA) is shown in Appendix IV Figure AIV.3 and AIV.4 with the assignment of products. 1 µL Crude reaction mixture containing internal standard (undecane; 1.2 mmol, 0.254 mL) was injected into a Hewlett Packard HP6890 Series auto-sampler GC system with column HP-1MS UI (30m*0.250mm*1.00µm). All the solvents have been assigned by comparing to their standard GC spectra. All the retention values of substrate and product to undecane have been determined using commercially available or isolated standard chemicals. More detailed information about heavy-ends is shown in Appendix IV.

Analysis conditions: 130 ºC (5 min), ramp 50 ºC / min to 300 ºC, 300 ºC (3.6 min) (12 min in total).

A GC trace of typical **hydroamidomethylation of pentenamides** is shown in Appendix IV Figure AIV.5, AIV.6, AIV.7, AIV.9 and AIV.10 with the assignment of products. 1 µL Crude reaction mixture containing internal standard (undecane; 1.2 mmol, 0.254 mL) was injected into a Hewlett Packard HP6890 Series auto-sampler GC system with column HP-1MS UI (30m*0.250mm*1.00µm). All the solvents have been assigned by comparing to their standard GC spectra. All the retention values of substrate and product to undecane have been determined using commercially available or isolated standard chemicals. More detailed information about heavy-ends is shown in Appendix IV.

Analysis conditions: 160 °C (3.3 min), ramp 30 °C / min to 300 °C, 300 °C (4 min) (12 min in total).

GC-MS Method: 1 µL Crude reaction mixture containing internal standard was injected into a GC HP7820 Series auto-sampler GC system with column DB-5MS UI (30m*0.250mm*1.00µm) equipped with MSD 5975 Agilent series. All the solvents have been ignored by comparing to their standard GC spectra. All the retention values of substrate and product to decane or undecane have been determined using commercially available or isolated standard chemicals.

Analysis conditions: 100 °C (2.5 min), 20 °C / min to 250 °C, 250 °C (5 min) (15 min in total).

5.4. References

[1] A. Corma, S. Iborra, A. Velty, *Chem. Rev.* **2007**, *107*, 2411.
[2] R. Weingarten, W. C. Conner, G. W. Huber, *Energy Environ. Sci.* **2012**, *5*, 7559.
[3] J. P. Lange, R. Price, P. M. Ayoub, J. Louis, L. Petrus, L. Clarke, H. Gosselink, *Angew. Chem. Int. Ed.* **2010**, *49*, 4479.
[4] J. Ritz, H. Fuchs, W. C. Kieczka, in *Morgan in Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, **2002**.
[5] I. Dodgson, K. Griffin, G. Barberis, F. Pignataro, G. Tauszik, *Chem. Ind.* **1989**, 830.
[6] Y. Wang, J. S. Zhang, X. C. Wang, M. Antonietti, H. R. Li, *Angew. Chem. Int. Ed.* **2010**, *49*, 3356.
[7] L. Liu, Y. Li, H. B. Wei, M. Dong, J. G. Wang, A. M. Z. Slawin, J. P. Li, J. X. Dong, R. E. Morris, *Angew. Chem. Int. Ed.* **2009**, *48*, 2206.
[8] K. Suzuki, T. Watanabe, S. I. Murahashi, *Angew. Chem. Int. Ed.* **2008**, *47*, 2079.
[9] Y. Ishii, S. Sakaguchi, *Catal. Today* **2006**, *117*, 105.
[10] A. B. Fernandez, M. Boronat, T. Blasco, A. Corma, *Angew. Chem. Int. Ed.* **2005**, *44*, 2370.

[11] K. I. Min, T. H. Lee, C. P. Park, Z. Y. Wu, H. H. Girault, I. Ryu, T. Fukuyama, Y. Mukai, D. P. Kim, *Angew. Chem. Int. Ed.* **2010**, *49*, 7063.
[12] J. S. Zhang, K. Wang, Y. C. Lu, G. S. Luo, *AlChE J.* **2012**, *58*, 925.
[13] S. S. Liu, A. Sen, R. Parton, *J. Mol. Catal. A: Chem.* **2004**, *210*, 69.
[14] R. Turgis, J. Estager, M. Draye, V. Ragaini, W. Bonrath, J. M. Leveque, *Chemsuschem* **2010**, *3*, 1403.
[15] S. G. Lee, J. Y. Shin, J. D. J., *ACS Catal.* **2013**, *3*, 525.
[16] J. Zhang, Y. Lu, K. Wang, L. G., *Ind. Eng. Chem. Res.* **2013**, *52*, 6377.
[17] R. J. van Putten, J. C. van der Waal, E. de Jong, C. B. Rasrendra, H. J. Heeres, J. G. de Vries, *Chem. Rev.* **2013**, *113*, 1499.
[18] D. J. Hayes, S. Fitzpatrick, M. H. B. Hayes, R. J. R. H., in *Biorefineries-Industrial Processes and Products: Status Quo and Future Directions*, Wiley-VCH, **2008**.
[19] J. C. Shen, C. E. Wyman, *AlChE J.* **2012**, *58*, 236.
[20] J. J. Bozell, L. Moens, D. C. Elliott, Y. Wang, G. G. Neuenscwander, S. W. Fitzpatrick, R. J. Bilski, J. L. Jarnefeld, *Resour. Conserv. Recy.* **2000**, *28*, 227.
[21] E. I. Gurbuz, S. G. Wettstein, J. A. Dumesic, *Chemsuschem* **2012**, *5*, 383.
[22] T. Runge, C. H. Zhang, *Ind. Eng. Chem. Res.* **2012**, *51*, 3265.
[23] M. G. Al-Shaal, W. R. H. Wright, R. Palkovits, *Green Chem.* **2012**, *14*, 1260.
[24] X. L. Du, Q. Y. Bi, Y. M. Liu, Y. Cao, K. N. Fan, *Chemsuschem* **2011**, *4*, 1838.
[25] Dumesic, J. A., Ruiz, J. C. Serrano, West, R. M., *US2010/324310 A1*, **2010**.
[26] F. M. A. Geilen, B. Engendahl, A. Harwardt, W. Marquardt, J. Klankermayer, W. Leitner, *Angew. Chem. Int. Ed.* **2010**, *49*, 5510.
[27] W. R. H. Wright, R. Palkovits, *Chemsuschem* **2012**, *5*, 1657.
[28] D. M. Alonso, S. G. Wettstein, J. A. Dumesic, *Green Chem.* **2013**, *15*, 584.
[29] X. L. Du, L. He, S. Zhao, Y. M. Liu, Y. Cao, H. Y. He, K. N. Fan, *Angew. Chem. Int. Ed.* **2011**, *50*, 7815.
[30] X. Hu, C. Z. Li, *Green Chem.* **2011**, *13*, 1676.
[31] W. Hoelderich, F. Naeumann, R. Fischer, *US Patent 5144061*, **1992**.
[32] F. Naeumann, W. Hoelderich, F. Merger, *US Patent 4879405*, **1989**.
[33] J. P. Lange, R. J. Haan, *WO2005058793 (A1)*, **2005**.
[34] J. P. Lange, J. Z. Vestering, R. J. Haan, *Chem. Commun.* **2007**, 3488.
[35] Boiling points for GVL: 207 °C; c-2-MP: 125 °C; t-2-MP: 144 °C; c-3-MP: 138 °C; t-3-MP: 155 °C; 4-MP: 128 °C; 4-MMP: 88 °C (39 Torr); 4-HMP: 105 °C (20 Torr).
[36] The calculation of the products distribution was achieved using calibration lines which were made of pure commercially available compounds.
[37] J. E. Baldwin, M. North, A. Flinn, M. G. Moloney, *Tetrahedron* **1989**, *45*, 1453.
[38] The calculation of the mixture of methyl pentenoates and products distribution as well as the selectivities before and after the reaction were determined by GC analysis using decane as an internal standard (for detailed information see appendix IV).
[39] E. Drent, R. Ernst, W. Jager, C. Krom, *WO2006/84892 A2*, **2006**.
[40] P. W. N. M. van Leeuwen, C. Claver, *Rhodium Catalyzed Hydroformylation* Kluwer Academic Publishers, **2000**.
[41] I. Ojima, A. Korda, *Tet. Lett.* **1989**, *30*, 6283.
[42] I. Ojima, A. Korda, W. R. Shay, *J. Org. Chem.* **1991**, *56*, 2024.
[43] R. P. J. Bronger, J. P. Bermon, J. Herwig, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Adv. Synth. Catal.* **2004**, *346*, 789.
[44] R. P. J. Bronger, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Organometallics* **2003**, *22*, 5358.
[45] L. A. van der Veen, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Angew. Chem. Int. Ed.* **1999**, *38*, 336.

[46] E. Zuidema, P. E. Goudriaan, B. H. G. Swennenhuis, P. C. J. Kamer, P. W. N. M. van Leeuwen, M. Lutz, A. L. Spek, *Organometallics* **2010**, *29*, 1210.
[47] The calculation of the mixture of pentenamides and products distribution as well as the selectivities before and after the reaction were determined by GC analysis using decane as an internal standard (for detailed information see appendic IV).
[48] L. E. Manzer, *WO Patent 2004/007421 A1*, **2004**.
[49] R. Kummer, H. W. Schneider, D. Zimmerling, in *US Patent 4561942 A*, **1985**.
[50] M. B. Bertrand, J. P. Wolfe, *Tetrahedron* **2005**, *61*, 6447.
[51] P. Gaudreault, C. Drouin, J. Lessard, *Can. J. Chem.* **2005**, *83*, 543.
[52] S. Knapp, A. T. Levorse, *J. Org. Chem.* **1988**, *53*, 4006.
[53] S. Nicolai, J. Waser, *Org. Lett.* **2011**, *13*, 6324.
[54] Q. F. Yang, J. E. Ney, J. P. Wolfe, *Org. Lett.* **2005**, *7*, 2575.
[55] S. A. King, *J. Org. Chem.* **1994**, *59*, 2253.