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Selective catalytic formation of unsaturated amino acids from petrochemicals and carbon dioxide—Application of high-throughput catalyst screening

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ABSTRACT

The atom economic hydroamination, the addition of an amine to an alkene, gained more and more importance as an "eco-friendly" alternative in amine synthesis. In this work the homogeneous catalytic 1,4-hydroamination of an unsaturated δ-lactone the 2-ethylidene-6-heptene-5-olide is investigated leading to a selective formation of an amino acid in a single step. The δ-lactone can be obtained by the telomerisation of the easily accessible 1,3-butadiene and the green house gas carbon dioxide. A new reactor concept is introduced which allows practical high-throughput catalyst screening with low costs. Variation of the metal precursors and the phosphorous ligands, optimisation of temperature and determinations of reaction rates leads to the catalyst system $Al(OTf)_3$/DPEphos, which combines high activity (TOF = 846 h^{-1}), no side products, low costs and low toxicity.

1. Introduction

Amines represent one of the most important classes of bulk and fine chemicals in chemical and pharmaceutical industry. They are used, for instance, as starting materials for solvents, dyes, surfactants, bactericides or anticorrosives and are applied as additives in textile industry, for pharmaceuticals and household chemicals. In 2006 amines and other nitrogen containing compounds were traded with a sales value of over € 5 billion in Germany. Thus their overall market share of organic industrial chemicals is in the range of about 12% [1].

This great importance demands not only economical but also ecological processes. Classic amine synthesis routes are often based on hazardous chemicals like hydrogen cyanide, chlorine and synthesis gas or are associated with the formation of large amounts of by-products. Additionally the starting materials are very expensive in many cases [2,3]. However, in recent time the atom economic hydroamination, the addition of an amine to an alkene, gained more and more importance as an "eco-friendly" alternative. This reaction is comparable to the addition of water or alcohols to alkenes which is already used in industry for many years. The control of the regioselectivity of these addition reactions ranks among the great challenges of catalysis [4].

For the hydroamination mainly two reaction routes are known: with monoalkenes a classic intermolecular as well as intramolecular 1,2-addition is reported leading to branched amines according to Markownikow's law [5]. On the other hand conjugated dienes are often subjected to an 1,4-addition (Fig. 1) [6].

However, the electronic properties of amines complicate this reaction [3]. Nevertheless many hydroaminations are described in literature using mostly homogeneous catalysts for activation. In this context almost all metals of the periodic table have been mentioned as catalyst. In contrast to other homogeneously catalysed reactions no universal catalyst has been found for the hydroamination like rhodium complexes for hydroformylation or palladium for telomerisation reactions. Depending on the nature of the substrates completely different metal complexes are used. Preferred transition metals are palladium [7,8], iridium [9,10], nickel [11], platinum [12–14], rhodium [15–17] and lanthanum [18] in combination with mostly bidentate phosphorous ligands. With annual 2000 t the Takasago process for the production of (−)-menthol from myrcene represents the largest technical realisation of a hydroamination reaction [19].

In this work we present a catalyst screening for the hydroamination of 2-ethylidene-6-heptene-5-olide, the δ-lactone **1**, which can be easily obtained by the telomerisation of 1,3-butadiene and carbon dioxide (Fig. 2) [20].

This telomer represents an interesting derivative of the green house gas carbon dioxide [21] and the easily accessible petrochemical 1,3-butadiene. It has one activated and one inactivated carbon–carbon double bond which should offer good conditions

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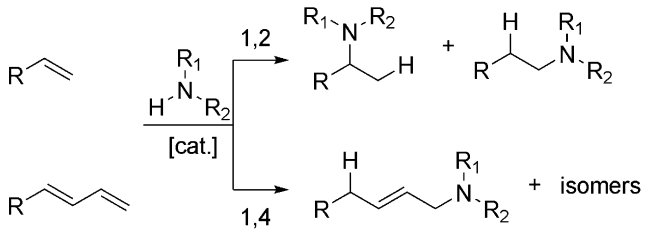

Fig. 1. General equation for the 1,2-addition of an amine to an alkene and 1,4-addition to a diene, respectively.

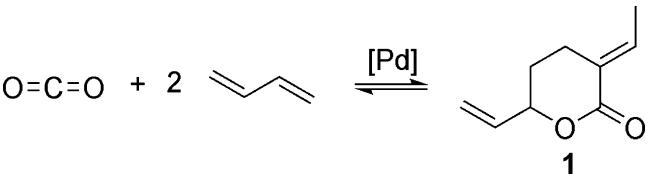

Fig. 2. Telomerisation of 1,3-butadiene with carbon dioxide.

for a hydroamination with a high selectivity in 1,2-additions. Furthermore regarding the free electron pairs at the ring-internal oxygen in conjugation with the α-double bond the δ-lactone may be considered as a diene analogous which allows 1,4-reaction routes.

After Inoue first reported the formation of the δ-lactone by telomerisation [22] Behr achieved selectivities higher than 90% by optimisation of the process [23]. Afterwards this reaction was transferred to miniplant scale which allows a continuous production combined with an efficient catalyst recycling [24]. Brehme and Behr then investigated the formation of several derivatives of this intermediate **1**. Via hydrogenation and hydroformylation reactions they synthesised various carboxylic acids, alcohols, diols, dicarboxylic acids and aldehydes of great industrial interest [25–27].

In this work a further derivatisation of the δ-lactone by hydroamination is described. Selective 1,4-addition of the model compound morpholine to the α-double bond of the δ-lactone allowed the synthesis of the amino acid **2** in a single step (Fig. 3). Starting from known catalyst systems [7–18] new more active and cheaper catalysts were determined by a high-throughput screening [28]. Furthermore the reaction conditions were optimised with respect to temperature and space-time-yield.

2. Experimental

2.1. General methods

All preparations and manipulations were performed under a dry, oxygen free argon atmosphere using standard Schlenk techniques. All solvents and chemicals were used without further purification unless otherwise noted. All chemicals were purchased from Acros and Strem. ^{1}H NMR and ^{13}C NMR were recorded with Bruker DPX-500 spectrometer at 300 K. Chemical shifts were reported on the δ-scale (ppm) with resonances upfield of Me_4Si. Elemental analyses were performed with a Leco analyser model CHNS-932. The IR spectrum was taken using Bruker IFS 28 in KBr disks at room temperature. The UV–vis spectrum of the amino acid **2** was recorded in a biochrom UV–vis photometer Libra S11/S12. The melting point of amino acid **2** was determined with a Büchi B-540 apparatus.

2.2. GC and HPLC analysis

GC analyses were carried out an a HP 6890 instrument equipped with a HP-5 column (30 m × 0.25 mm × 0.25 μm). GC-MS analyses were carried out on a Hewlett-Packard 5973 (70 eV).

The parameters for GC and GC-MS were as given:

Carrier gas (N_2) flow	1.2 mL/min; 30 cm/s
Injection temperature	275 °C
Detector temperature	275 °C
Oven temperature program	60 °C-3 min-10 °C/min–80 °C-3 min-40 °C/min–250 °C–7.75 min

HPLC analyses were carried with a Merck-Hitachi L-7100 pump, a Merck-Hitachi L-7200 with 100 μL injection volume, a Merck-Hitachi L-7350 oven and a Merck-Hitachi L-7400 UV-detector. The column used was a Merck-LiChroprep® RP18 (25–40 μm) with a length of 250 mm and an inner diameter of 4.6 mm. The eluent was acetonitrile/water 3:1 with 1 vol.% triethylamine. The samples were analysed at 300 K at a detector wavelength of 268 nm.

2.3. General procedure for the hydromamination of the δ-lactone (*1*) with morpholine

5.0 mmol δ-lactone **1**, 5.0 mmol morpholine, 0.011 mmol Pt(cod)Cl_2 and 0.18 mmol DPEphos are dissolved in 30 mL anhydrous toluene using the standard Schlenk techniques. The reaction mixture was transferred into a stainless steel reactor. The reactor was pressurised with 5 bar of argon and the mixture was heated to the designated temperature, for instance, 100 °C. After a reaction time of 24 h the reactor is cooled down to room temperature, the pressure is released and the mixture was analysed by GC and HPLC.

2.4. Isolation and characterisation of 2-ethyliden-7-morpholinohept-5-enoic acid (*2*)

The crude product was purified by column chromatography (silica gel, ethanol/triethylamine 9:1) to give a mixture of the *E* and *Z* isomers of **2**. mp 87.5–90 °C (stereoisomer 1), 97.5–101 °C (stereoisomer 2), IR (KBr, cm^{-1}): 3570 (b), 2966 (m), 2921 (m), 2860 (m), 2476 (b), 1993 (b), 1684 (m), 1646 (m), 1457 (w), 1385 (m), 1292 (w), 1113 (s), 998 (w), 976 (w), 864 (m), 772 (m). UV: λ (A_{max}) = 268 nm. MS (*m*/*z*): 239 (M+, 3%), 224 (8), 211(3), 194 (2), 183 (21), 168 (45), 154 (15), 140 (6), 135 (3), 126 (44), 110 (78), 100 (34), 96 (17), 87 (100), 81 (42), 77 (11), 67 (38), 55 (62). Elemental analysis: calculated for $C_{13}H_{21}NO_3$: C, 65.3; H, 8.8; N, 5.9; found: C, 64.9; H, 9.1; N, 5.7.

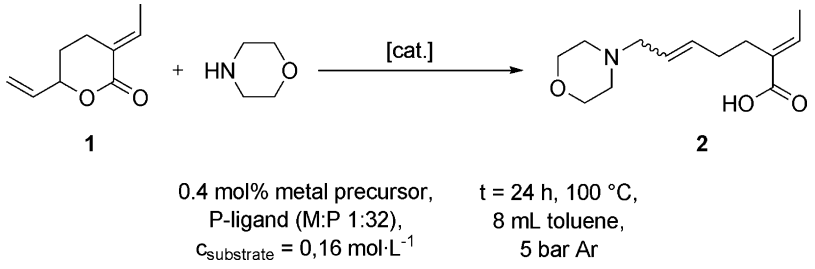

Fig. 3. Hydroamination of the δ-lactone and reaction conditions for screening.

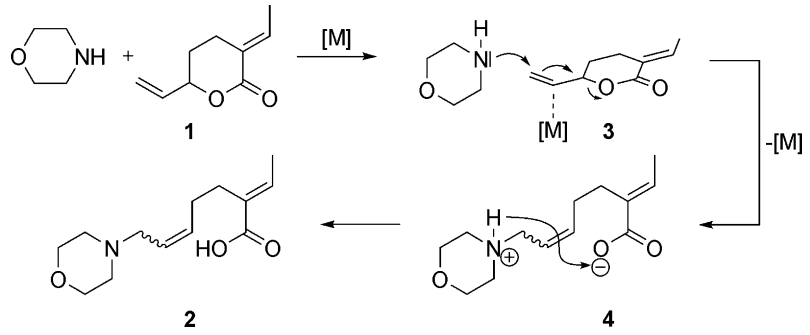

Fig. 4. Suggested mechanism of amino acid formation in presence of a "soft" lewis acid.

2.4.1. (E)-isomer

^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.66 (d, $^3J(^1H–^1H) = 7.2$ Hz, 3H, CH(CH_3)), 2.10 (m, 2H, CH–CH_2–CH_2), 2.29 (m, 2H, CH–CH_2–CH_2), 2.47 (broad signal, 4H, N(CH_2)$_2$), 2.93 (m, 2H, CH_2–N(CH_2)$_2$), 3.66 (t, $^3J(^1H–^1H) = 4.4$ Hz, 4H, CH_2–O–CH_2), 5.39 (m, 1H, N–CH_2–CH=CH), 5.57 (m, 1H, N–CH_2–CH=CH), 6.70 (q, $^3J(^1H–^1H) = 7.1$ Hz, 1H, $CH(CH_3)$), 10.46 (broad signal, 1H, COOH). ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 14.1 (s, 1C, CH(CH_3)), 26.2 (s, 1C, CH–CH_2–CH_2), 31.7 (s, 1C, CH–CH_2–CH_2), 52.4 (s, 2C, N(CH_2)$_2$), 60.4 (s, 1C, CH_2–N(CH_2)$_2$), 65.9 (s, 2C, CH_2–O–CH_2),124.1 (s, 1C, N–CH_2–CH=CH), 134.4 (s, 1C, C–COOH), 135.4 (s,1C, $CH(CH_3)$), 135.8 (s,1C, N–CH_2–CH=CH), 171.6 (s, 1C, COOH).

2.4.2. (Z)-isomer

^{1}H NMR (500.13 MHz, $CDCl_3$): δ 1.66 (d, $^3J(^1H–^1H) = 7.2$ Hz, 3H, CH(CH_3)), 2.10 (m, 2H, CH–CH_2–CH_2), 2.29 (m, 2H, CH–CH_2–CH_2), 2.47 (broad signal, 4H, N(CH_2)$_2$), 2.93 (m, 2H, CH_2–N(CH_2)$_2$), 3.66 (t, $^3J(^1H–^1H) = 4.4$ Hz, 4H, CH_2–O–CH_2), 5.39 (m, 1H, N–CH_2–CH=CH), 5.57 (m, 1H, N–CH_2–CH=CH), 6.70 (q, $^3J(^1H–^1H) = 7.1$ Hz, 1H, $CH(CH_3)$), 10.46 (broad signal, 1H, COOH). ^{13}C NMR (125.77 MHz,$CDCl_3$): δ 14.1 (s, 1C, CH(CH_3)), 26.2 (s, 2C, CH–CH_2–CH_2), 44.5 (s, 1C, CH_2–N(CH_2)$_2$), 52.4 (s, 2C, N(CH_2)$_2$), 65.9 (s, 2C, CH_2–O–CH_2),124.1 (s, 1C, N–CH_2–CH=CH), 134.4 (s, 1C, C–COOH), 135.4 (s,1C, $CH(CH_3)$), 135.8 (s,1C, N–CH_2–CH=CH), 171.6 (s, 1C, COOH).

3. Results and discussion

3.1. Investigations with the catalyst system iridium/DPEphos

The investigations were started with the catalyst system of iridium and DPEphos (see Fig. 7). Fig. 3 shows the reaction conditions of the high selective conversion of the δ-lactone **1** into the amino acid **2**. The δ-lactone could be converted by 98%, and the amino acid **2** was obtained with 96% isolated yield. The *E*/*Z*-mixture was characterised by MS, ^{1}H NMR, ^{13}C NMR and IR (see Section 2). A pressure of 5 bar argon is necessary to keep the volatile morpholine in solution.

Dependent on the kind of the catalytic metal used we suggest two different mechanisms for the formation of the amino acid. "Soft" Lewis acids like Ir^+ attack presumably the α-double bond (**3**) forming an allyl complex. During formation of the allyl complex the C—O bond is broken and the nucleophilic attack of the amine is favoured (Fig. 4). According to the NMR the resulting amino acid is not existent as a zwitterion **4**. For that reason the proton migrates forming the carboxylic acid **2**. Kinetic studies of this reaction exhibit that the conversion of the substrate is faster than the formation of the product. It indicates that there is an ionic intermediate **4**, which is invisible in the GC. Only after the last step of our suggested mechanism the product can be observed in the gas chromatogram.

Further experiments (see below) show also an activity of "hard" Lewis acids. "Hard" Lewis acids normally do not generate a π-complex but rather coordinate to hard atoms, which lead to the suggestion of a second mechanism (Fig. 5). The metal complex increases the draw of electrons by coordination to the oxygen atoms **5**, so that the nucleophilic attack of the amine is facilitated. The further steps are comparable to the mechanism of the "soft" Lewis acids.

3.2. New reactor concept

Although the concentration of the iridium catalyst is relatively low, the price of the metal precursor represents a big disadvantage considering the economical point of view. Furthermore the reaction time of 24 h is too long for a technical realisation. Hence we developed a new reactor for facilitating a high-throughput screening under inert conditions to find a suitable catalyst with the requested properties.

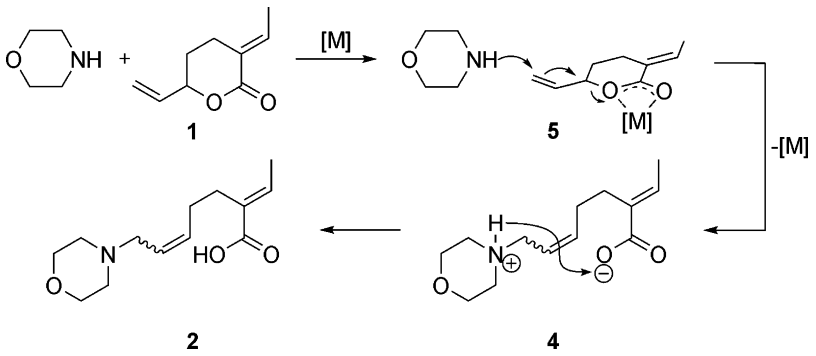

Fig. 5. Suggested mechanism of amino acid formation in presence of a "hard" lewis acid.

Fig. 6. Multiplex-reactor consisting of six pressure reactors and a frame for heating in an oil bath.

The developed screening set consists of six reactors (Fig. 6), which are arranged on a frame for heating in a conventional oil bath. In every reactor a solution of 8 mL is stirred by a magnetic stirring bar. For safety reasons a bursting disk is assembled, which releases pressures over 50 bar. A ball valve controls the in- and output. Every reactor can be filled by a single separate adapter. With the exception of the reactor pot and the holder for bursting disk this multiplex-reactor only consists of commercially available components.

The new reactor system for high-troughput screening affords easy cleaning (no fixtures, minimisation of contaminations), low catalyst costs as a result of the low reaction volume and negligible short times for heating up (reaction begins with dipping into the oil bath). The costs are considerably lower than for conventional reactors.

3.3. *Catalyst screening*

In a first step of the catalyst screening the metal precursor and the ligand are varied under the reaction conditions of the standard system (Fig. 3). Fig. 7 gives an overview of the ligands used. The next step contains an optimisation of the reaction temperature, before the activity of the selected catalyst systems is determined in the last step.

Under the screening conditions an experiment without any catalyst only shows a conversion of 6%. Furthermore the reaction affords no conversion with the organic acids methanesulfonic acid, *p*-toluenesulfonic acid and phthalic acid. So acid-catalysis can be excluded.

The low conversion in all experiments using metal precursors without any addition of ligands indicates that the modification of the catalyst by ligands is essential (Tables 1–3). Only the precursor $Ce(OTf)_3$ catalyses the reaction with a conversion of 42% without any supplementary ligand. The cheap monodentate ligand

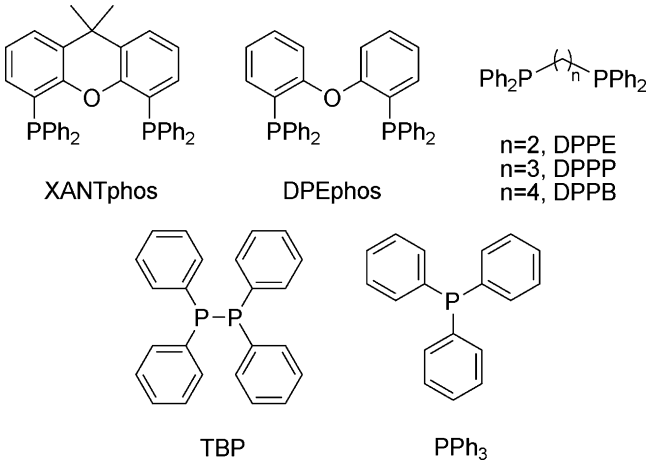

Fig. 7. Overview of ligands used.

Table 1
Conversions (%) of δ-lactone **1** with exclusive formation of amino acid **2**, determined by GC[a]

Ligand	$[Rh(cod)_2]BF_4$	$Pd(CF_3CO_2)_2$	$Ir(acac)(CO)_2$
No ligand	–	21	12
PPh_3	6	96[b]	53
DPPE	4	26	4
DPPP	4	100[b]	7
DPPB	27	96[b]	14
DPEphos	50	96[b]	**96**
XANTphos	8	94[b]	21
TBP	–	33	17

[a] Conditions: 0.4 mol% precursor (M), P-ligand (M:P 1:32), 8 mL toluene, $c_{\delta\text{-lactone}} = 0.16\ mol\ L^{-1}$, δ-lactone:morpholine 1:1, 5 bar Ar, $t = 24$ h, $T = 100\ ^\circ C$.
[b] Isomerisation of δ-lactone.

Table 2
Conversions (%) of δ-lactone **1** with exclusive formation of amino acid **2**, determined by GC[a]

Ligand	$PtCl_2$	$Fe(acac)_2$	$Co(acac)_2$
No ligand	3	0	4
PPh_3	**90**	7	14
DPPE	6	0	0
DPPP	24	4	6
DPPB	**97**	11	56
DPEphos	**91**	**94**	**94**
XANTphos	**90**	12	14
TBP	24	–	–

[a] Conditions: see Table 1.

triphenylphosphine achieves good conversions only in combination with $Pd(CF_3CO_2)_2$ (96%) and $PtCl_2$ (90%), whereas the use of palladium leads to the isomerisation of the δ-lactone to the known γ-lactones [29] in very low concentrations (Fig. 8).

Table 3
Conversions (%) of δ-lactone **1** with exclusive formation of amino acid **2**, determined by GC[a]

Ligand	$Ni(acac)_2$	$Zr(OTf)_4$	$Ce(OTf)_3$
No ligand	1	–	42
PPh_3	12	15	30
DPPE	22	6	6
DPPP	22	0	4
DPPB	46	16	26
DPEphos	73	71	**96**
XANTphos	8	11	8
TBP	11	–	–

[a] Conditions: see Table 1.

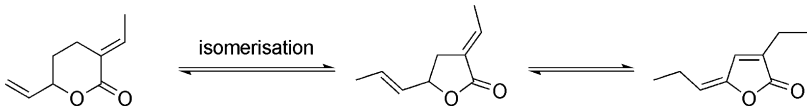

Fig. 8. Isomerisation of the δ-lactone to the γ-lactones.

By using alkyl-bridged bisphosphine ligands (DPPE, DPPP, DPPB) the conversion increases with growing chain length. Therewith results of the hydroamination already described by Hartwig could be confirmed [17]. In the rhodium-catalysed hydroamination of 3-arylpiperidines Hartwig observed a conversion of 84% by using the butyl-bridged ligand (DPPB) instead of a conversion of 0% by using the propyl-bridged ligand (DPPP). Satisfactory results in the hydroamination of the δ-lactone with the alkyl-bridged ligands were only obtained with the $PtCl_2$/DPPB catalyst (97%, Table 2).

The usage of the ether-bridged ligand DPEphos seems to be the best choice for the 1,4-hydroamination of the δ-lactone **1**. With DPEphos nearly all metals afford a high conversion in the range of 90–95%. From an industrial point of view the cheap catalyst $Al(OTf)_3$/DPEphos with a conversion of 94% is of special interest. In combination with DPEphos the lanthanides $Ce(OTf)_3$ and $La(OTf)_3$, respectively, also achieve conversions of 96 and 94%.

A small modification of the flexible ether-skeleton of DPEphos to the more rigid skeleton of XANTphos causes a significant loss of conversion. With a catalyst of $La(OTf)_3$ and the ligand XANTphos the δ-lactone was converted only with 38%. However, the $PtCl_2$ system could guarantee a high conversion (90%) with both ligands. The bisphosphine ligand TBP yields only moderate conversions (11–33%).

In order to affirm the results of the new multiplex-reactor some comparative experiments were additionally made with commercially available 70 and 300 mL reactors, which could attest that the new reactor concept works with a low fault tolerance (Table 4). The conversions (*X*) and the yields (*Y*) of these experiments were determined by HPLC. Noteworthy is the remarkably high selectivity (*S*) towards the amino acid **2** up to 99%.

3.4. Variation of the temperature

Variation of the temperature shows that 100 °C is the optimum for most catalyst systems. At room temperature the cobalt, iron and iridium catalysts show no activity (Fig. 9). By usage of $Co(acac)_2$ a rise of conversion (55–97%) is observed with increasing temperature (70–120 °C). The iron and iridium catalysts are inactive at 70 °C in contrast to the cobalt-system. For the iron catalyst an increase in temperature from 100 to 120 °C is not reasonable because of an additional low formation of by-products and the lowered conversion of 70%.

Table 4
Conversions (%) of the δ-lactone **1** with morpholine in a commercial 70 mL-reactor; yields and selectivities of the amino-acid **2**[a]

Precursor	Ligand	*X* (%)[b]	*Y* (%)[c]	*S* (%)[c]
$Fe(acac)_2$	DPEphos	76	74	97
$PtCl_2$	XANTphos	74	71	96
$Zr(OTf)_4$	DPEphos	94	92	98
$[Rh(cod)_2]BF_4$	DPEphos	72	71	99
$Co(acac)_2$	DPEphos	92	91	99
$Pt(cod)Cl_2$	DPEphos	99	95	96
$La(OTf)_3$	DPEphos	85	83	98
$Ce(OTf)_3$	DPEphos	89	88	99

[a] Conditions: see Table 1.
[b] Determined by GC.
[c] Determined by HPLC.

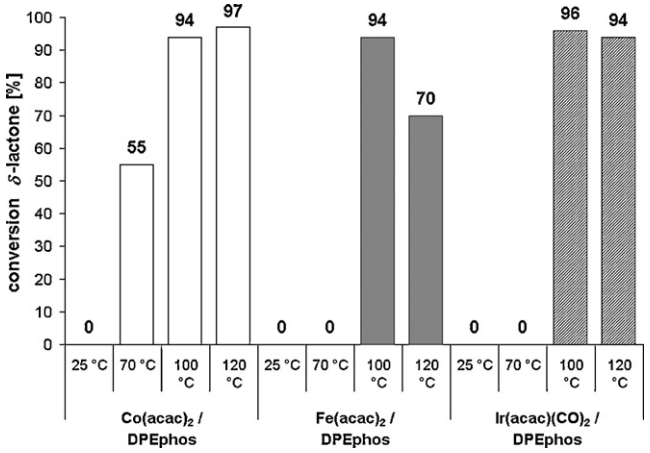

Fig. 9. Catalyst activity in dependence on temperature.

By usage of lanthanoids only a low temperature effect at high temperatures (100 and 120 °C, Fig. 10) can be observed. Both lanthanum and cerium provide conversions from 93 to 98%.

There is hardly any influence of temperature variation if $Pt(cod)Cl_2$ is used as catalyst (92–100% conversion). The Pt(II)-catalyst is the most active of the catalysts used due to his constant activity even at room temperature. The complete conversion at 120 °C is caused by the isomerisation of the δ-lactone as side reaction (Fig. 8).

3.5. Determination of reaction rates

At last the reaction rate was determined to achieve a considerable reduction of reaction time. For this purpose an autoclave (70 mL) was used which allowed continuous sampling. Turn-over frequencies (TOF (h^{-1})) are compared with each other in order to determine the catalyst activity. The reference time for calculating the TOF is that time, at which a constant conversion is obtained. With the catalyst system $Ir(acac)(CO)_2$/DPEphos the effects of

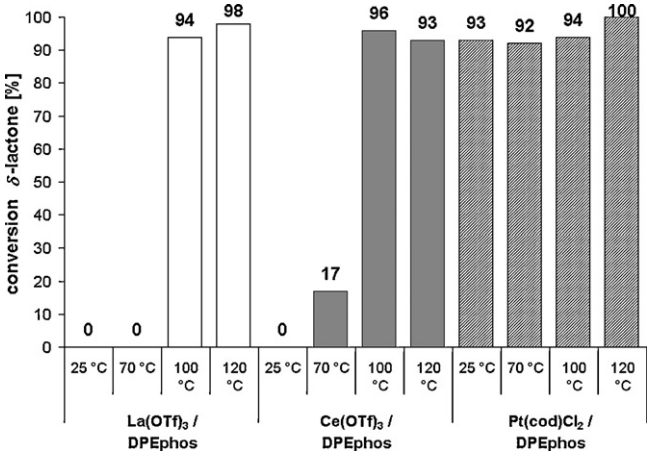

Fig. 10. Catalyst activity in dependence on temperature.

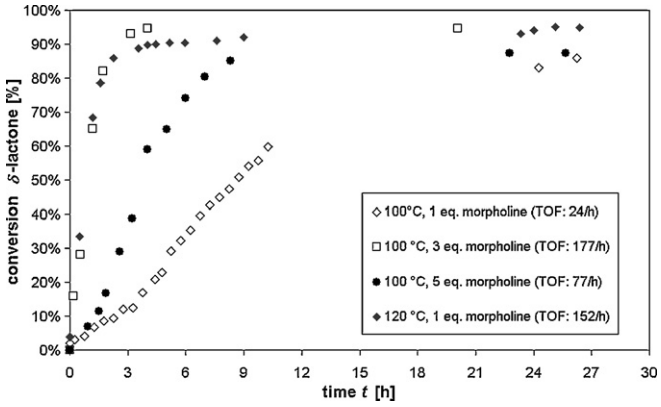

Fig. 11. Activity of the catalyst system $Ir(acac)(CO)_2$/DPEphos in dependence on time (conditions: 0.4 mol% $Ir(acac)(CO)_2$, DPEphos (Ir:P 1:32), $c_{\delta\text{-lactone}} = 0.16\ mol\ L^{-1}$, 5 bar Ar, 70 mL toluene).

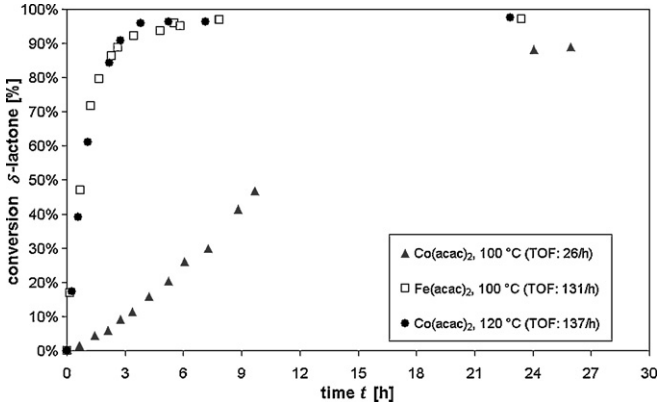

Fig. 12. Activity of cobalt and iron catalysts in dependence on time (conditions: 0.4 mol% precursor (M), DPEphos (M:P 1:32), $c_{\delta\text{-lactone}} = 0.16\ mol\ L^{-1}$, 1 eq. morpholine, 5 bar Ar, 70 mL toluene).

temperature and morpholine concentration on the reaction rate (Fig. 11) were investigated.

The curve (◊) represents the reaction rate at standard conditions (0.4 mol% catalyst, 100 °C, 1 eq. morpholine). The morpholine concentration has a significant influence on the conversion rate. An increase to the three-fold amount of morpholine results in a conversion of 95% with a TOF of 177 h^{-1}. However, a further increasing to the five-fold amount decreases the reaction rate (within 8 h to a conversion of 85%). As expected the high amine concentration deactivates the catalyst by coordinative saturation. A temperature of 120 °C has a similar influence like the three-fold morpholine concentration: A conversion of 90% can be observed within 4.5 h. Obviously the hydroamination of the δ-lactone is very sensitive to any changes in reaction conditions, which emphasises the necessity of a high-throughput screening for optimisation.

A higher TOF than with iridium can be obtained by using $Pt(cod)Cl_2$ as catalyst. At 100 °C the TOF rises to 374 h^{-1}, after heating up to 120 °C the TOF increases to the highest observed value of 1192 h^{-1}, unfortunately caused by the isomerisation of the δ-latone as side reaction.

An alternative to the high-priced iridium and platinum catalysts are $Co(acac)_2$ and $Fe(acac)_2$ (Fig. 12). The formation of the amino acid **2** proceeds slower by using $Co(acac)_2$ than $Ir(acac)(CO)_2$. $Fe(acac)_2$ causes a considerably higher activity at the same temperature. With $Co(acac)_2$ a comparable conversion can only be achieved by rising the temperature to 120 °C.

Although the reaction time has already been reduced to 4 h with the cobalt and iron catalysts, a further remarkable time reduction could be achieved with $Al(OTf)_3$. This main group metal provides a considerable conversion of 94% after only 50 min. With $Al(OTf)_3$ a suitable catalyst for the hydroamination of the δ-lactone was found which could find application in industry. This catalyst combines a high activity (TOF = 846 h^{-1}), with low costs and low toxicity. Table 5 summarizes the results of the examinations of the reaction rate.

Table 5
Overview of catalyst activities[a]

Precursor	Ligand	T (°C)	X (%)[b]	t (h:min)	TOF (h^{-1})
$Zr(OTf)_4$	DPEphos	100	94	1:00	590
$Co(acac)_2$	DPEphos	100	89	25:57	26
$Co(acac)_2$	DPEphos	120	96	5:15	137
$Fe(acac)_2$	DPEphos	100	96	5:31	131
$Al(OTf)_3$	**DPEphos**	**100**	**94**	**0:50**	**846**
$La(OTf)_3$	DPEphos	100	100	1:30	363
$Ce(OTf)_3$	DPEphos	100	96	4:31	159
$Ir(acac)(CO)_2$	DPEphos	100	86	26:45	24
$Ir(acac)(CO)_2$[c]	DPEphos	100	95	4:01	177
$Ir(acac)(CO)_2$[d]	DPEphos	100	85	8:18	77
$Ir(acac)(CO)_2$	DPEphos	120	90	4:26	152
$Pt(cod)Cl_2$	DPEphos	100	99	1:59	374
$Pt(cod)Cl_2$	DPEphos	120	98[e]	0:37	1192

[a] Conditions: see Table 1.
[b] Determined by GC.
[c] 3 eq. morpholine.
[d] 5 eq. morpholine.
[e] Isomerisation of δ-lactone.

4. Conclusions

In conclusion, we presented the 1,4-hydroamination of the δ-lactone **1**, a telomer of 1,3-butadiene and carbon dioxide, leading to unsaturated highly functionalised amino acids. As a result of a systematic catalyst screening realised by a new reactor concept we were able to optimise the reaction conditions with a technical implementation in mind. The optimisation led to the best catalyst system $Al(OTf)_3$/DPEphos, which combines high activity (TOF = 846 h^{-1}), no side products, low costs and low toxicity. In addition catalyst systems from "soft" metal atoms and DPEphos are also able to catalyse the reaction in a promising manner: $Ir(acac)(CO)_2$ (TOF = 177 h^{-1}), $Pt(cod)Cl_2$ (374 h^{-1}) and $Fe(acac)_2$ (131 h^{-1}). In further works we will investigate the recycling of the catalyst and the usage of other amines.

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