



# Selective Synthesis of Primary Amines by Kinetic-based Optimization of the Ruthenium-Xantphos Catalysed Amination of Alcohols with Ammonia

Christian Heider,<sup>[a]</sup> Dominik Pietschmann,<sup>[a]</sup> Dieter Vogt,<sup>[a]</sup> and Thomas Seidensticker\*<sup>[a]</sup>

The selective synthesis of primary amines directly from several alcohols and ammonia using a homogeneous catalyst based on  $\text{HRuCl}(\text{CO})(\text{PPh}_3)_3$  and Xantphos is presented. The key to success was the detailed understanding of all mutually influencing parameters such as temperature, ammonia excess, and substrate concentration. These studies were supported by the determination of the kinetics, which allowed the reaction order to be calculated as 0.7. Furthermore, the kinetic model derived from the mechanism was confirmed. After measuring reaction profiles for all influencing parameters, optimized conditions

were obtained, which finally allowed the amination of aliphatic, cyclic, as well as primary and secondary alcohols with selectivities to the desired primary amine exceeding 90% at quantitative alcohol conversion with only minimal formation of the undesired secondary amines. Furthermore, the catalytic activity of the commercially available and robust Xantphos system was drastically improved, corresponding to a turnover frequency (TOF)  $> 60 \text{ h}^{-1}$  after 30 minutes and a turnover number (TON) of 120.

## Introduction

Amines are used in a wide variety in the chemical industry, for instance, to produce fine chemicals, dyes, agrochemicals, pharmaceuticals, and polymers.<sup>[1,2]</sup> Different catalytic amine syntheses have thus been established, such as nitrile hydrogenation, reductive amination of carbonyl compounds, and the heterogeneously catalyzed amination of alcohols.<sup>[3,4]</sup> Especially primary, terminal amines are important intermediates due to their high reactivity. However, this reactivity poses challenges to their synthesis, particularly on a large scale. For the synthesis of primary amines, a direct and selective reaction of ammonia with different bulk chemicals would be beneficial. But this higher reactivity of primary amines compared to ammonia favors the formation of secondary or even tertiary amines in consecutive reactions, thereby lowering overall selectivity. Furthermore, harsh conditions typically applied in the heterogeneously catalyzed alcohol amination ( $T > 200^\circ\text{C}$ ) are also detrimental to a highly selective reaction.<sup>[4]</sup>

Besides heterogeneous systems, homogeneous catalysts for the amination of alcohols are also known on the laboratory scale, primarily based on noble metals like Ru and Ir or other transition metals like Mn. The reaction follows the so-called borrowing hydrogen mechanism, in which water is the only co-product (Figure 1).<sup>[5]</sup>

In principle, alcohol amination is characterized by very high chemoselectivity. Side reactions are suppressed by the low concentration of reactive intermediates like the carbonyl compound and the imine/enamine. However, the suppression of consecutive reactions forming undesired secondary and tertiary amines is challenging, especially in synthesizing primary amines employing ammonia. The formation of secondary amines in the first place proceeds via two different pathways (Figure 2), both following the borrowing hydrogen mechanism.<sup>[6-9]</sup> The first way (alcohol amination, Figure 2, A) also starts with the dehydration (I) of the alcohol to the carbonyl compound. However, in the second step, instead of

[a] C. Heider, D. Pietschmann, Prof. D. Vogt, Dr. T. Seidensticker  
TU Dortmund University  
Department for Biochemical and Chemical Engineering  
Laboratory of Industrial Chemistry  
Emil-Figge-Straße 66  
44227 Dortmund (Germany)  
E-mail: thomas.seidensticker@tu-dortmund.de  
Homepage: <https://tc.bci.tu-dortmund.de/>

Supporting information for this article is available on the WWW under <https://doi.org/10.1002/cctc.202200788>

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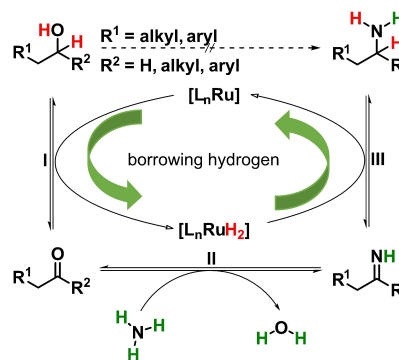


Figure 1. Borrowing hydrogen mechanism for the amination of alcohols with ammonia affording primary amines.

ammonia, the primary amine reacts in the condensation with the aldehyde or ketone (II), forming a secondary enamine and water. In the other way (deaminative coupling, Figure 2, B), the primary amine is catalytically dehydrogenated to the corresponding imine (I), which reacts with another primary amine in a condensation reaction via a hemiaminal. The corresponding secondary imine/enamine is formed, liberating ammonia as the co-product (II).<sup>[7–9]</sup> Catalytic hydrogenation (III) of the secondary enamine/imine in both routes finally yields the secondary amine. Tertiary amines can principally be formed similarly, starting from the alcohol or secondary amine. However, their formation is highly dependent on the sterical demand of the substrate. Beller and co-workers, as well as our research group, reported that secondary and tertiary amines can also be catalytically cleaved with ammonia following deaminative coupling.<sup>[2,10]</sup>

The homogeneously catalyzed amination of alcohols offers some advantages for the synthesis of primary amines compared to heterogeneous systems: The use of molecular hydrogen is not required, and milder reaction conditions can be used, leading to more selective syntheses of primary amines, as shown by the groups of Milstein, Fujita, Beller and Schaub, and our research group.<sup>[6,11,12–17]</sup>

For example, different studies on the amination of 1-octanol (1) with ammonia (Table 1) already showed that the combination of ruthenium precursors like  $\text{HRuCl}(\text{CO})(\text{PPh}_3)_3$  and unique ligands like the Milstein-Ligand (L1) and Triphos (L2) yield primary amines with high selectivities, good catalytic activity only using a slight ammonia excess (Table 1, entries 1 and 2).<sup>[12,15–17]</sup> Using L1, low catalyst loadings of 0.1 mol% led to quantitative conversion with an excellent selectivity towards *N*-octylamine (2) of 95%. Using L2 with 0.2 mol% catalyst loading and 180 °C reaction temperature, the selectivity of 2 was 92%. However, the general usability of these systems is rather limited, either by their generally very high sensitivity to moisture and air or limited availability.

Nevertheless, using commercially available and robust catalyst systems, up to now, only secondary alcohols like cyclohexanol have been converted into primary amines with preparatively satisfying selectivities exceeding 90%.<sup>[6,13]</sup> The direct amination of primary alcohols with ammonia yielding primary amines in high selectivities is still complicated and often limited to:



Thomas Seidensticker studied chemistry at TU Dortmund University and received his doctorate in 2016 under the supervision of Prof. Dr. Arno Behr. Since 2017, he has been a junior research group leader in the group with Prof. Dr. Dieter Vogt. His research is dedicated to sustainable process design for homogeneous transition metal catalysts, including the development of innovative recycling methods and the conversion of renewable resources. Since January 2021, he has been setting up his own junior research group “renewlysis” at TU Dortmund University combining catalysis with renewable resources.

- poor catalyst activity/productivity
- huge ammonia excesses
- high selectivities only at low conversion

An excellent example of these limitations is the direct amination using the commercial Xantphos ligand (L3, Table 1, entries 3 and 4). Moderate selectivities of 79% could be achieved using a high catalyst loading of 3 mol% and a 60-fold ammonia excess.<sup>[18]</sup> With a catalyst loading of just 0.1 mol%, the catalytic activity/productivity could be increased, but only 77% of the desired primary amine was obtained, while the conversion was only 30%.<sup>[17]</sup> Generally, the selectivity is even more decreased at higher conversions due to a higher concentration of the reactive primary amine (2).

This comparison shows that combining the advantages of unique ligands such as L1 and L2 with the benefits of commercial ligands such as L3 would be desirable to develop a reliable and robust synthesis method for primary amines from ammonia and alcohols. However, this combination does not yet exist since no in-depth studies have been carried out. Therefore, we are convinced that detailed insights into the individual impact of the reaction parameters and mutual influences, combined with further insights through kinetic studies, will lead to an improved understanding of the reaction. Thus, a highly selective synthesis method for various primary amines from alcohols and ammonia using a robust and commercially available catalyst will be available.

## Results

As a model reaction, the amination of 1-octanol (1) with ammonia, using  $\text{HRuCl}(\text{CO})(\text{PPh}_3)_3$  and L3 to produce the desired *N*-octylamine (2) was chosen. A reaction temperature of 170 °C, a catalyst loading of 0.83 mol%, and a ruthenium to phosphorus ratio of 1:4 was chosen based on our latest publication on alcohol amination.<sup>[14]</sup> An excess of 20 eq of ammonia was used, like in our latest publication on the amination with ammonia.<sup>[6]</sup> Under these conditions, a reaction profile was recorded (Figure 3) by taking samples at regular intervals. After 4 h, 1 was fully converted at a selectivity to the primary amine 2 of 80%, which is in accordance with previous investigations.<sup>[12,18]</sup> Furthermore, the reaction profile shows that the primary amine was formed directly from the start of the reaction, while the secondary amine could be detected after 90 min. Interestingly, the selectivity here is stable even with the increasing conversion of 1, which is different from the literature.<sup>[12]</sup> Neither the intermediate aldehyde (1-octanal) nor the corresponding primary imine could be detected, but traces of the secondary enamine. After the complete conversion of 1, the yield and selectivity of 2 did not change, indicating that the formation from 3 by a reaction of 1 and 2 (Figure 2, A) is more favored than the deaminative coupling of two mols 2 (Figure 2, B). To prove this hypothesis, samples were also taken after 21, 42, and 72 h. The selectivity towards 2 dropped to 68, 61, and 53%, respectively, due to the formation of the secondary amine 3. The deaminative coupling is thus relatively slow under the

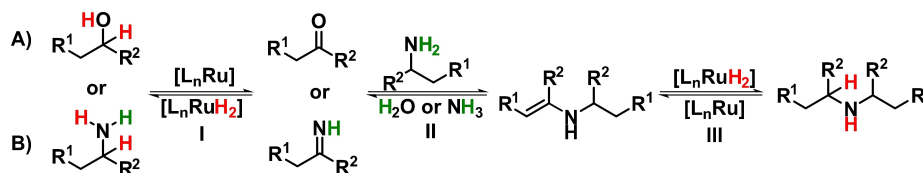


Figure 2. Formation of secondary amines by A) alcohol amination and B) deaminative coupling.

**Table 1.** Ruthenium-catalyzed amination of 1-octanol (1) with ammonia by HRuCl(CO)(PPh<sub>3</sub>)<sub>3</sub> and Ligands L1–L3. Conversion (X) and selectivity (S) based on 1-octanol.

Entry [reference]	Ligand	TON	t [h]	T [°C]	Ru [mol%]	NH <sub>3</sub> [eq]	X [%]	S [%]
1, [22]	L1	990	12	155	0.1	7	99	95
2, [22]	L2	495	12	180	0.2	6	99	92
3, [29]	L3	298	12	155	0.1	6	30	77
4, [30]	L3	33	20	140	3	60	99	79

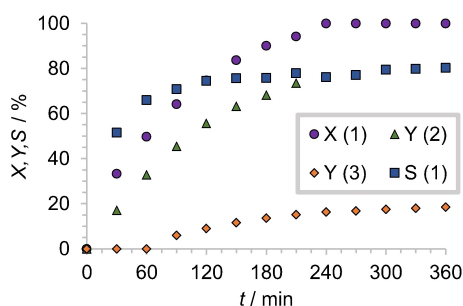


Figure 3. Reaction profile for the amination of 1-octanol (1) with ammonia. Conditions: 1-octanol (15 mmol), ammonia (8.46 mL, 300 mmol, 20 eq), HRuCl(CO)(PPh<sub>3</sub>)<sub>3</sub> (0.125 mmol, 0.83 mol%), Xantphos (0.249 mmol, 1.66 mol%), *t*-amyl alcohol (37.5 mL), 170 °C, 15 bar Ar. Conversion (X), yield (Y), and selectivity (S) were determined via GC-FID with *n*-dodecane as an internal standard. The numbers in parentheses refer to the numbers of the molecules in the text.

chosen reaction conditions compared to alcohol amination. Still, no tertiary amine 4 was produced.

Next, we optimized the reaction conditions by detailed studies on the start concentration, catalyst loading, ammonia excess, and temperature. The reaction rate constant  $k$  was calculated for all reactions under different conditions. Thus we gain a more profound knowledge of the reaction, and besides the selectivity towards 2, the activity of the catalyst could be described, too. For doing so, general integration of the rate equation for calculating  $k$  was used (Equation 1, for integration, see SI). The reaction was thus determined to be of 0.7 order. This non-integer reaction order was expected since only the dependency on the alcohol amination was considered. Due to

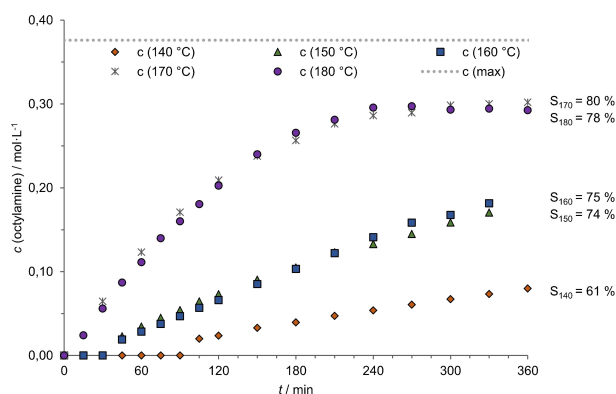
this limitation, all main and consecutive reactions are included. In 1985, KIJENSKI *et al.* described the heterogeneously catalyzed reaction of 1-octanol with *N,N*-dimethylamine as a first-order reaction whereby the reaction only depends on the alcohol concentration ( $c_{\text{octanol}}$ ), which does not precisely fit our reaction order. However, when using dimethylamine, no consecutive reactions are possible.<sup>[19]</sup>

$$-\frac{dc_{\text{octanol}}}{dt} = k \cdot c_{\text{octanol}}^a \quad (1)$$

For the reaction shown in Figure 3,  $k$  was determined to be  $1.034 \cdot 10^{-4} \text{ (mol/L)}^{0.3} \cdot \text{s}^{-1}$ . Therefore  $(1/c_{\text{octanol}})^{0.3}$  was plotted against time  $t$  and  $k$  resulting from the slope. This reaction was repeated two more times, giving the same results.  $k$  could thus be determined as  $k = 1.120 \cdot 10^{-4} \pm 0.191 \text{ (mol/L)}^{0.3} \cdot \text{s}^{-1}$ . Thereby  $k$  was only calculated for the first 120 min.

The impact of the temperature was investigated to increase the selectivity towards 2. In the literature, temperatures between 120 to 150 °C are commonly used. However, to achieve a highly selective synthesis, the splitting of higher amines (Figure 2) needs to be addressed, which usually requires higher temperatures, like 170 °C. We thus increased the temperature to 180 °C (Figure 4) to allow the splitting of secondary and, possibly, tertiary amines. In addition, a faster reaction is also expected due to higher catalytic activity at elevated temperatures.

For all reactions, the reaction rate constant  $k$  was calculated (Table S2, see SI). By comparing the  $k$  values, it was found that the reaction at 170 °C was 7.5 times faster than that at 140 °C



**Figure 4.** Concentration profiles of octylamine (2) in dependency of the reaction temperature. Conditions: 1-octanol (15 mmol), ammonia (8.46 mL, 300 mmol, 20 eq), HRuCl(CO)(PPh<sub>3</sub>)<sub>3</sub> (0.125 mmol, 0.83 mol%), Xantphos (0.249 mmol, 1.66 mol%), *t*-amyl alcohol (37.5 mL), 15 bar Ar. Concentrations (*c*) were determined via GC-FID with *n*-dodecane as internal standard. Selectivity (*S*) at final concentration. Subscript numbers at the selectivity (*S*) indicate the temperature of 2 (*X*, *S* = 100%). The dotted line indicates the maximum possible concentration of 2 (*X*, *S* = 100%).

and four times faster than the reactions at 150 and 160 °C. Further temperature increase up to 180 °C did not influence the reaction performance. The selectivity of 2 increases with increasing temperature, indicating that higher reaction temperatures are beneficial for the selective synthesis of primary amines directly from alcohols and ammonia. Furthermore, the selectivity for the reactions below 170 °C will decrease with a longer reaction time because only incomplete conversion is achieved after 6 hours. In addition, it can also be seen that at reaction temperatures below 170 °C, the reaction starts slowly. Based on previous mechanistic investigations, alcohol is necessary for activating the ruthenium-Xantphos system.<sup>[6]</sup> Due to the defined reaction start, ensured by a dropping funnel, the activation must first occur at the time *t* = 0 min and is clearly favored at 170 and 180 °C. This investigation shows that temperature has a significant impact on selectivity, as well as on catalytic activity.

Overall, pseudo first-order rate constants are helpful for a rough comparison. However, only a mechanism-based full kinetic model, including all relevant partial reactions of the whole reaction network, will allow valid predictions. Therefore, a comprehensive reaction network was established (Figure 5). Starting from the primary alcohol 1, the primary amine 2 can be formed due to the borrowing hydrogen mechanism. The overall reaction is described by the reaction rate constant *k*<sub>1</sub>. The splitting of amines with water, represented by *k*<sub>2</sub>, was not considered in the calculation, because of the low water amount, compared to the amount of ammonia in the solution. The reactive intermediates 5, 6 and 7 were not detectable via GC-FID, making it impossible to describe all reaction rate constants labeled with roman numerals. For the formation of the secondary amine 3, two pathways are possible. The first starts from 1, following the alcohol amination (Figure 2, A). This overall reaction from 1 and 2 to 3 is described by *k*<sub>4</sub>, whereas *k*<sub>3</sub> is negligible because of the very low water concentration

compared to the high ammonia excess. The second possible pathway (Figure 2, B) is the deaminative coupling of two mols 2 to 3 and ammonia described by *k*<sub>5</sub>. Hereby the splitting of the secondary amine with ammonia, represented by *k*<sub>6</sub>, is also considered because of the vast ammonia excess. The reaction to the tertiary amine 4 is not shown, as it was not detected in any reaction. But in theory, the mechanism would be the same, but instead of the primary amine 2, the secondary amine 3 would react with the primary imine 6 or the aldehyde 5.

Due to the measurable concentration of 1, 2 and 3, three main differential equations were posted:

$$\frac{dc_{\text{octanol}}}{dt} = -k_1 \cdot c_{\text{octanol}} - k_4 \cdot c_{\text{octanol}} \cdot c_{\text{octylamine}} \quad (2)$$

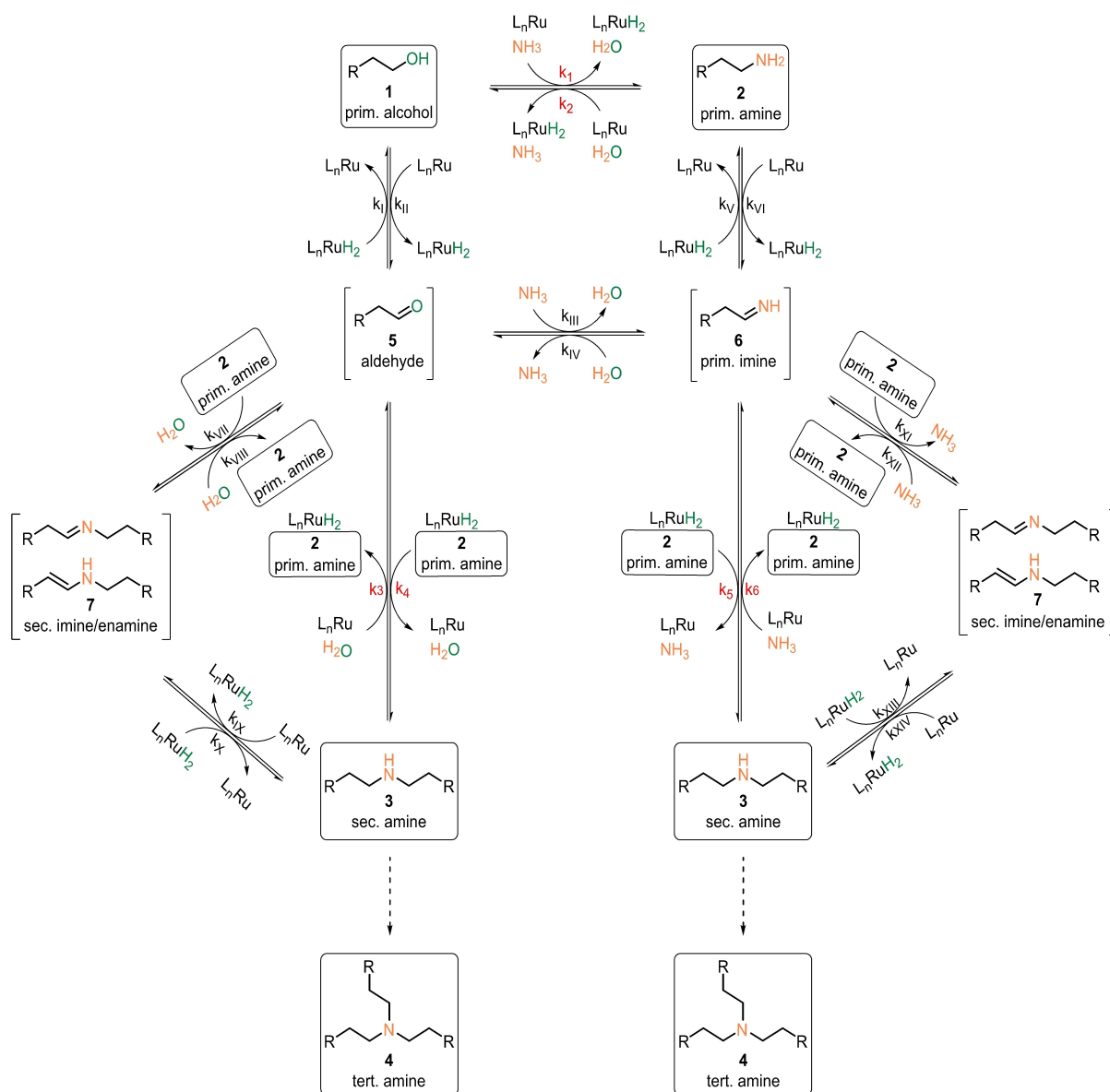
$$\frac{dc_{\text{octylamine}}}{dt} = k_1 \cdot c_{\text{octanol}} - k_4 \cdot c_{\text{octanol}} \cdot c_{\text{octylamine}} + 2k_6 \cdot c_{\text{dioctylamine}} - k_5 \cdot c_{\text{octylamine}}^2 \quad (3)$$

$$\frac{dc_{\text{dioctylamine}}}{dt} = k_4 \cdot c_{\text{octanol}} \cdot c_{\text{octylamine}} - k_6 \cdot c_{\text{dioctylamine}} + k_5 \cdot c_{\text{octylamine}}^2 \quad (4)$$

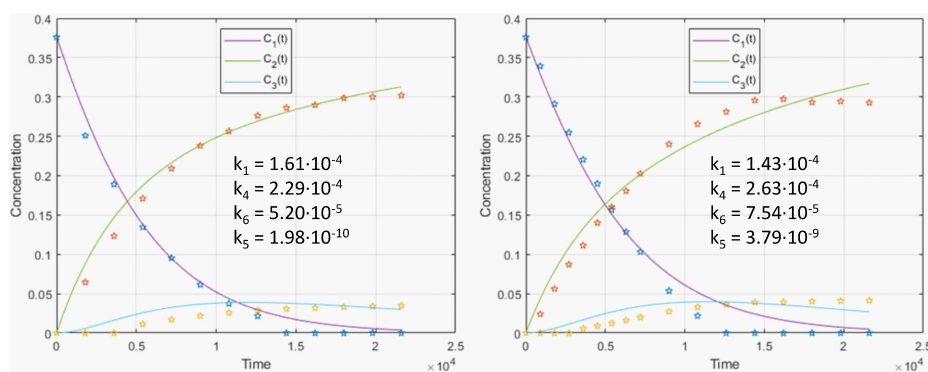
The concentration of ammonia was neglected because the change over time is marginal due to the high excess. Furthermore, reactions initiated by water instead of ammonia were ignored since the amount of ammonia is much higher than that of water. As a result, four unknown rate constants are described by the concentration of 1, 2 and 3. Thus, no trivial mathematical solution exists. Therefore, MATLAB and the ode45 solver were used to determine the reaction rate constants by a numerical approximation based on the measured values (Figure 6).

It is evident that *k*<sub>5</sub> is much smaller than the other constants, as the deaminative coupling of two mols of 2 is less favored when the alcohol is still present in the reaction mixture, which was also observed in the first reaction (Figure 3). *k*<sub>1</sub>, representing the reaction of 1 with ammonia, has a slightly lower value at 180 °C compared to 170 °C. However, by comparing *k*<sub>4</sub> (deaminative coupling of 1 and 2), the value at 170 °C is lower than that for 180 °C. Both *k*<sub>1</sub> and *k*<sub>4</sub> are values for the reaction of 1, so by adding these up and dividing by each other, a quotient of 0.96 is calculated (170 °C values are the numerator). For 180 °C, *k*<sub>6</sub>, the splitting of 3 into two mols of 2, is 1.5 times greater than the reaction at 170 °C. This fact shows that the splitting of secondary and tertiary amines is favored at elevated temperatures. But also, the secondary amine formation by following the alcohol amination (*k*<sub>4</sub>) is larger by a factor of 1.2 at 180 °C. In the end, the faster formation of 2 and the splitting lead to the same selectivity compared to 170 °C (Figure 4). With the available data on the temperature dependency, the activation energy could be calculated according to ARRHENIUS to 89 kJ·mol<sup>-1</sup>.

In the next step, the initial concentration of 1 varied between 5–25 mmol (Figure 7). With the method of initial rates, the reaction order was found to be 0.67, which fits the order determined previously by the integral method.

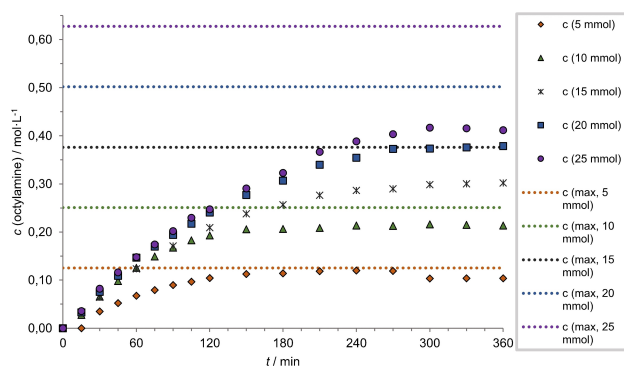


**Figure 5.** Reaction network of the ruthenium-catalyzed amination of primary alcohols (1-octanol if R = C<sub>6</sub>H<sub>13</sub>). Structures in rectangles were detected via GC-FID, whereas structures in brackets were not.



**Figure 6.** The approximation results with MATLAB for the reaction at 170 (left) and 180 °C (right). The x-axis shows the time  $t$  in seconds, and the y-axis shows the concentration  $c$  in  $\text{mol} \cdot \text{L}^{-1}$ . For conditions, see Figure 4.  $c_1$  = octanol,  $c_2$  = octylamine and  $c_3$  = dioctylamine.





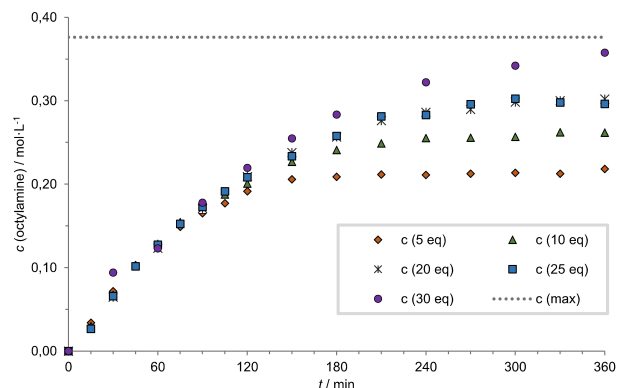
**Figure 7.** Concentration profiles of octylamine (**2**) in dependency of its initial concentration. Conditions: 1-octanol (5–25 mmol), ammonia (8.46 mL, 300 mmol, 12–60 eq), HRuCl(CO)(PPh<sub>3</sub>)<sub>3</sub> (0.125 mmol), Xantphos (0.249 mmol), *t*-amyl alcohol (37.5 mL), 170 °C, 15 bar Ar. Concentrations (*c*) were determined via GC-FID with *n*-dodecane as internal standard. Values in parentheses indicate the amount of alcohol used. The dotted lines indicate the maximum possible concentrations of **2** (*X*, *S* = 100%).

Moreover, as expected, the selectivity decreases with decreasing ammonia excess; the consecutive reactions are favored at increasing **2**:NH<sub>3</sub> ratios. For example, a selectivity of only 65% was reached using the highest amount of **1** (25 mmol, purple) with 12 eq ammonia. On the other hand, by decreasing the amount of **1** from 20 mmol to 15 to 10 mmol, the selectivity towards **2** increases from 76% to 80% and 86%, respectively.

Interestingly, with 5 mmol **1** (orange), corresponding to 60-fold excess of ammonia, the selectivity is almost perfect after 240 min and slightly decreases to 95%, representing the highest value achieved so far. Compared to Beller and co-workers (Table 1, entry 4), who also used 60 eq of ammonia, our selectivity is 15% higher on a larger scale. This fact shows that the ratio of ammonia and alcohol significantly impacts the selectivity toward the primary amine.

The next step is thus to investigate the influence of ammonia at a constant concentration of **1**. Therefore, the excess of ammonia was varied, while 15 mmol of **1** was used (Figure 8). As before (Figure 7), the selectivity increases with higher ammonia excess. Five equivalents of ammonia led to only 58% of the desired primary amine **2**, whereas 10 eq gave the desired *N*-octylamine with 70% selectivity. By increasing the excess to 20 and 25 eq, respectively, 80% selectivity of **2** could be reached. While using 30 eq of NH<sub>3</sub>, excellent selectivities of 95% were obtained, which are equal to selectivities typically achieved using the Milstein-Ligand (**L1**, Table 1, entry 1).

The synthesis of a primary amine using a commercial and robust catalyst system, under non-dry or degassed conditions, in very high selectivities was now feasible. Furthermore, we increased the catalytic activity compared to existing Xantphos-based systems (Table 1, entry 4). The turnover number (TON) could be increased to 120, which is a factor of 4.5. Due to this higher catalytic activity, complete conversion was already achieved after only 6 hours. By decreasing the ammonia excess, the reaction time decreases too, but at the expense of selectivity. So, in the end, a compromise between high

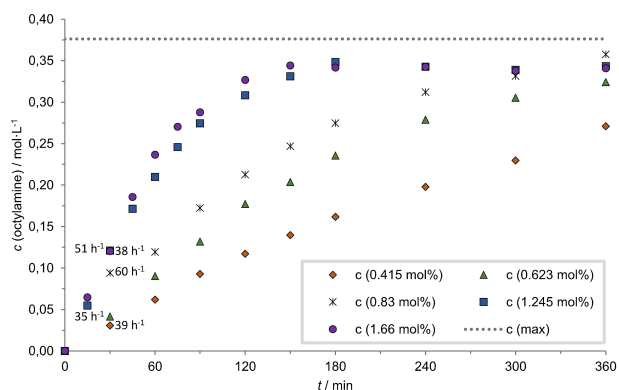


**Figure 8.** Concentration profiles of octylamine (**2**) in dependency of the ammonia excess. Conditions: 1-octanol (15 mmol), ammonia (2.12–12.69 mL, 75–450 mmol, 5–30 eq), HRuCl(CO)(PPh<sub>3</sub>)<sub>3</sub> (0.125 mmol, 0.83 mol%), Xantphos (0.249 mmol, 1.66 mol%), *t*-amyl alcohol (37.5 mL), 170 °C, 15 bar Ar. Concentrations (*c*) were determined via GC-FID with *n*-dodecane as internal standard. The dotted line indicates the maximum possible concentration of **2** (*X*, *S* = 100%). Subscript numbers at the selectivity (*S*) indicate the ammonia equivalent.

selectivities and high catalytic activity must be chosen. At 30 eq ammonia, excellent selectivity towards the primary amine can be achieved, and a further increase of ammonia excess is not needed.

Besides the selectivity, the behavior of the reaction in the first 90 minutes seems to be independent of the ammonia excess. However, after a critical octylamine concentration, the formation gets slower, so there is a crucial point where the ratio of **2** and ammonia determine the selectivity of the reaction.

Due to the equal speed of the octylamine formation in the first 90 minutes, it is beneficial to unravel whether a faster or slower reaction caused by higher or lower catalyst loading can affect the selectivity of the reaction. Notably, the selectivity is constant over the reaction time (Figure 3). Therefore, the precursor concentration (HRuCl(CO)(PPh<sub>3</sub>)<sub>3</sub>) was varied next (Figure 9) at 6 hours reaction time, as this was sufficient to reach quantitative conversion with 0.83 mol% (Figure 8, *c* (30 eq)). It was expected that the reaction would become faster with higher catalyst loadings. To compare the catalytic activity, the turnover frequency after 30 minutes (TOF<sub>30</sub>) was calculated for the primary amine formation. With 0.83 mol%, a TOF<sub>30</sub> of 60 h<sup>-1</sup> could be reached. As expected, the reaction became slower at the two lower precursor loadings. However, while using 0.623 mol%, 93% conversion, with a selectivity of 92%, was achieved, corresponding to a TOF<sub>30</sub> of 35 h<sup>-1</sup>. Using even less catalyst gave only 79% conversion of **1** at a still high selectivity of > 90%. The TOF<sub>30</sub> was 39 h<sup>-1</sup>, 35% less than at 0.83 mol%. Increasing the reaction time to 21 h led to complete conversion at the same selectivity. With the 1.5-fold catalyst loading, the reaction became twice as fast, and complete conversion was reached after only 3 hours. But the TOF<sub>30</sub> decreased to 51 h<sup>-1</sup> because of the higher catalyst loading. The further increase of the catalyst had no significant influence on the reaction performance, but the TOF<sub>30</sub> again decreased to 38 h<sup>-1</sup>, respectively. However, the solubility of the ligand was



**Figure 9.** Concentration profiles of octylamine (2) in dependency of the catalyst loading. Conditions: 1-octanol (15 mmol), ammonia (12,69 mL, 450 mmol, 30 eq), HRuCl(CO)(PPh<sub>3</sub>)<sub>3</sub> (0.0625–0.25 mmol, 0.415–1.66 mol%), Xantphos (0.125–0.50 mmol, 0.83–3.32 mol%), *t*-amyl alcohol (37.5 mL), 170 °C, 15 bar Ar. Concentrations (c) were determined via GC-FID with *n*-dodecane as internal standard. Values next to the measuring points represent the TOF for 30 min. The dotted line indicates the maximum possible concentration of 2 (X, S = 100%).

no longer given when using 1.5 and 2 times the amount of catalyst, which is why solids were present in the reactor after the completion of the reaction. With all tested amounts, selectivities greater than 90% were achieved, which shows that the catalyst loading has no impact on the selectivity. In other words, the speed of the reaction doesn't determine selectivity at high conversions. For the following reactions, 0.83 mol% of HRuCl(CO)(PPh<sub>3</sub>)<sub>3</sub> was used.

After we could successfully improve the performance and selectivity of the reaction due to in-depth parameter investigation, different substrates (c) were tested to see if the developed conditions are suitable as a reliable and useful tool for the selective synthesis of primary amines from various alcohols and ammonia. Therefore, linear, cyclic, benzylic and branched alcohols were tested, as well as diols and alcohols with ester moieties (Table 2). In addition to primary alcohols, secondary alcohols were also tested. When using secondary alcohols, which are less reactive compared to primary ones, only 20 instead of 30 equivalents of ammonia were used. The time to reach complete conversion is indicated for each substrate. High selectivities were achieved using the optimized condition for the linear, aliphatic alcohols 1-hexanol to 1-hexadecanol (8a–8e). All reactions showed the same performance, but for the alcohols higher than 1-decanol, the products precipitated upon cooling the reactor to room temperature. The branched 2-ethyl hexyl alcohol (8f) reacted slightly slower, giving complete conversion after only 7 hours, with a selectivity of 96%.

For 1,12-dodecanediol (8g), good selectivities of the bisaminated product of 91% were reached. The main byproduct was monoaminated alcohol. Methyl 12-hydroxy laurate (8j) as renewable alcohol was converted into the primary amine with 95% selectivity. The benzylic alcohol (8h) was also successfully aminated. However, selectivity was not constant: First, some secondary amine was formed, then split into two mols of 9h. The secondary alcohol cyclohexanol (8i) was also aminated

**Table 2.** Results from the substrate screening in the amination of several alcohols with ammonia.

$\text{R-OH} + \text{NH}_3 \xrightarrow[\text{t-amyl alcohol, 170 }^\circ\text{C}]{[\text{Ru}]}$ $\text{R-NH}_2$	
$\text{(CH}_2\text{)}_2\text{CH}_2\text{NH}_2$	$\text{(CH}_2\text{)}_4\text{CH}_2\text{NH}_2$
9a, <i>t</i> = 5.5 h, S = 95%	9b, <i>t</i> = 5 h, S = 91%
$\text{(CH}_2\text{)}_5\text{CH}_2\text{NH}_2$	$\text{(CH}_2\text{)}_6\text{CH}_2\text{NH}_2$
9c, <i>t</i> = 6 h, S = 91%	9d, <i>t</i> = 4 h, S = 93%
$\text{(CH}_2\text{)}_7\text{CH}_2\text{NH}_2$	$\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$
9e, <i>t</i> = 4 h, S = 91%	9f, <i>t</i> = 7 h, S = 96%
$\text{H}_2\text{N-CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH}_2$	$\text{C}_6\text{H}_5\text{CH}_2\text{NH}_2$
9g, <i>t</i> = 3 h, S = 91%	9h, <i>t</i> = 5 h, S = 98%
$\text{C}_6\text{H}_{11}\text{NH}_2$	$\text{CH}_3\text{OOC-CH}_2\text{-CH}_2\text{-CH}_2\text{-CH}_2\text{-NH}_2$
9i, <i>t</i> = 10 h, S = 94%	9j, <i>t</i> = 6 h, S = 95%

Conditions: 8a–j (15 mmol, 7.5 mmol for diols), ammonia (8,459–12,69 mL, 300–450 mmol, 20–30 eq), HRuCl(CO)(PPh<sub>3</sub>)<sub>3</sub> (0.125 mmol, 0.83 mol%), Xantphos (0.249 mmol, 1.66 mol%), *t*-amyl alcohol (37.5 mL), 170 °C, 15 bar Ar. Conversion and selectivity (S) were determined via GC-FID with *n*-dodecane as internal standard. The reaction times *t* represent the time to reach quantitative alcohol conversion.

with excellent selectivities of 94%, even when only 20 eq of ammonia were used. As expected, the reaction time increases for the less reactive secondary alcohol. In all reactions of the substrate screening, again, no tertiary amines were formed. The main byproducts were always the secondary amine and traces of the secondary enamine.

## Conclusions

This study presents the highly selective synthesis of primary amines from alcohols and ammonia using a commercial ruthenium-Xantphos catalyst system under non-dry or degassed conditions. Selectivities of up to 95% were reached for several primary and secondary, as well as aliphatic, cyclic and benzylic alcohols. Furthermore, we achieved high TONs at complete conversion and, at the same time, excellent selectivities, which is not reported for the employed system. The key to success was in-depth studies of the influencing parameters combined with mechanism-based kinetic studies. These studies showed that the selectivity of direct aminations with ammonia highly depends on the ratio of primary amine, alcohol and ammonia, as well as the reaction temperature since the splitting of secondary and tertiary amines – which is also able under these reaction conditions – requires elevated temperatures. Based on these results, we could devise a simple, generally applicable

protocol for the selective synthesis of various primary amines on the gram scale.

## Experimental Section

**Typical amination reaction using ammonia:** All reactions were performed in a 75 mL stainless steel autoclave equipped with a magnetic stirrer and a dropping funnel. Before preparation, the reactor was flushed with argon, and afterwards, the ruthenium precursor and the ligand were filled into the autoclaves. The reactor was closed and inertized by three vacuum/argon cycles. Subsequently, 32.5 mL solvent was added to the reactor in an argon counterflow using a syringe. Next, 5 mL of the solvent and the alcohol were mixed and added to the dropping funnel. Afterward, the reactor was pressurized with 15 bar argon, and the ammonia was precisely dosed as liquid using a syringe pump. The reaction mixture was heated to 170 °C and stirred at 900 rpm for 20 minutes. The pressure settled at about 42 bar. After reaching the temperature, the reaction was started by adding the alcohol from the dropping funnel by opening the respective ball valve. Manual samples were periodically taken for analysis using a dip tube. After the reaction time, the autoclaves were cooled, depressurized, and emptied, and the samples were prepared for further investigations via GC-FID.

## Acknowledgments

C.H. is grateful to the Evonik Foundation for their generous financial support. We thank M. Sc. Kevin Hares for assisting in ligand synthesis. Open Access funding enabled and organized by Projekt DEAL.

## Conflict of Interest

The authors declare no conflict of interest.

## Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Keywords:** amination · diamines · homogeneous catalysis · kinetics · renewable feedstocks

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Manuscript received: June 22, 2022  
Revised manuscript received: July 28, 2022  
Accepted manuscript online: August 3, 2022  
Version of record online: August 25, 2022