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The impact of the nature of amine reactants in the palladium catalyzed conversion of phenol to *N*-substituted anilines

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ABSTRACT

Anilines and cyclohexylamines are currently produced from fossil feedstocks. Phenol would be an attractive alternative feedstock that can be obtained from renewable resources. We herein clarify the influence of the amine on the course of the amination of phenol using a hydrogen borrowing strategy. Amines can in this case act as a reductant which can be dehydrogenated to initiate the partial hydrogenation of phenol which is required for the reaction to take place. The nature of the amine reactant can have a larger effect than the presence of additional reductants like sodium formate. The results in this report do not only present a method for the amination of phenol without addition of an extra reductant, but also rationalize the reactivity of amines in their reaction with phenol.

1. Introduction

Aniline and its derivatives are important building blocks for electronic materials, polymers and active pharmaceutical ingredients [1,2]. The production of anilines is industrially realized by nitration of arenes and subsequent gas-phase hydrogenation of the nitro-arenes to the anilines [3]. In case of *N*-functionalized anilines, the anilines undergo a further step of alkylation [4], or the substituted anilines are synthesized from aryl halides by the Buchwald-Hartwig reaction. Currently, anilines are produced starting from petrochemicals; however, biobased phenols, as main building block in lignocellulosic biomass, are ideal alternative starting materials. An industrial process for the amination of phenol to aniline was investigated decades ago. The reaction took place at elevated temperatures between 350 °C and 500 °C in the gas phase using an acidic SiO_2-Al_2O_3 and later ZSM-5 catalyst, yet it was not brought to industrial implementation [5].

Recently, a new approach for the amination of phenol has come forward. This pathway proceeds *via* the reductive coupling of phenols with amines, catalyzed by Pd/C and results in the formation of *N*-alkylated cyclohexylamines (Scheme 1A) [6–8]. Three steps take place in one pot, namely the partial reduction of phenol to cyclohexanone using sodium formate, the formation of an *N*-alkylated cyclohexylimine and the further reduction towards the corresponding cyclohexylamine. However, anilines are more interesting for many applications than their saturated counterparts. The reaction of cyclohexanone with amines for the formation of anilines is well known [9–11], and was envisioned to be employed for the direct conversion of phenol to anilines [12]. By using the right, lower, amount of sodium formate as reductant and increasing the reaction temperature it is possible to hydrogenate phenol to cyclohexanone and dehydrogenate the imine towards the anilines in one pot (Scheme 1B) [12]. This strategy was extended to the conversion of benzylphenylethers, where the *O*-benzyl bond is cleaved and the corresponding *N*-alkyl cyclohexylamine is formed along with toluene [8]. Further, saturated *N*-heterocycles were employed in the amination of phenol, in which the six-ring of phenol is hydrogenated towards a cyclohexyl moiety using an added reductant, coupled to the pyrrolidine or indoline and eventually dehydrogenated towards *N*-cyclohexyl indole or *N*-cyclohexyl pyrrole [13].

Another approach towards the synthesis of phenylcyclohexylamines is the self-condensation of cyclohexylamine under dehydrogenative conditions in oxygen using a $PdAu/Al_2O_3$ alloyed catalyst [14]. Cyclohexylamine is first dehydrogenated to cyclohexylimine, which then reacts with another molecule of cyclohexylamine; after further dehydrogenation, phenylcyclohexylamine is obtained. Although oxygen is used in this conversion, dehydrogenation of the cyclohexylimine is known to proceed even in an inert atmosphere [11], which formally results in the evolution of hydrogen. In literature, some trends regarding the nature of the amines have been observed, such as the possibility to react anilines to *N*-cyclohexylanilines, but not to dehydrogenated *N*-phenylanilines [6,12]. However, there was not yet a structured investigation of the role of the amine in the direct phenol amination. Further, all

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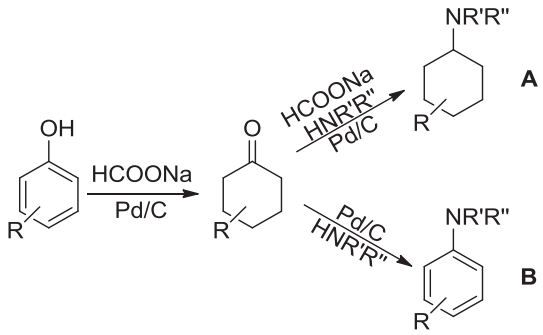
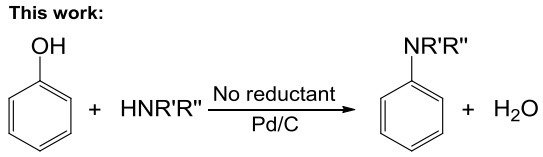


Scheme 1. Reaction sequence for the amination of phenol towards alkylated cyclohexylamines (A) and anilines (B). The product distribution can be controlled by adapting the reaction conditions [6,12].



Scheme 2. Phenol to aniline conversion in the absence of a reductant.

methods for amination of phenol via cyclohexanone as intermediate so far required an added reductant; yet an approach without addition of such a reductant would be desirable.

We envisioned that an initial dehydrogenation of the amine could be sufficient to provide the reducing equivalents for the intermediate hydrogenation to cyclohexanone, which reacts with an amine and is dehydrogenated again during the formation of the aniline. In this way, this sequence can be considered as a 'hydrogen borrowing strategy', which is reversed in comparison with the usual hydrogen borrowing. Reducing equivalents must first be provided by dehydrogenation of the amine to hydrogenate the phenol to cyclohexanone, and not by the dehydrogenation of the alcohol as is common in classical hydrogen borrowing reactions [15].

We herein report the direct reaction of phenol with amines for the formation of *N*-alkylsubstituted anilines in the absence of any external reductant using Pd/C as catalyst (see Scheme 2). We elucidate the effect of the amine structure on the yield and discuss the influence of sodium formate as reductant.

2. Results and discussion

The direct conversion of phenol to *N*-alkylated anilines over palladium on carbon was investigated first in the presence, and later in the absence of sodium formate.

2.1. Amination of phenol with cyclohexylamine

As a first model reaction, we investigated the reaction of phenol with cyclohexylamine for the synthesis of *N*-phenylcyclohexylamine (Fig. 1). A slight excess of cyclohexylamine, viz. 1.4 eq with respect to phenol, and sodium formate (1.5 eq) were employed. The latter serves as reductant to initiate the reaction under a nitrogen atmosphere. Toluene was used as solvent, as it was shown to be suitable for the phenol to aniline conversion [12,16].

The concentration-time profile (Fig. 1a) of the reaction shows that phenol (PhOH; initially 0.2 M, defined as 100 mol%) was converted gradually within the first 11 h of the reaction to form *N*-phenylcyclohexylamine (PhCHA) as main product with steadily increasing concentrations up to 113 mol% after 30 h. Dicyclohexylamine (DCA) was formed as by-product with increasing concentration until a value of 20 mol% after 6 h; thereafter its concentration decreased to 6 mol% at the end of the reaction. Cyclohexylamine (CHA) was consumed at a higher rate than phenol, which is the result of the net reaction of 2 molecules cyclohexylamine towards the secondary amines PhCHA or DCA, with loss of NH_3 through an aminal intermediate. This also explains why the final concentration of PhCHA is higher than the initial phenol concentration; product yield therefore is higher than for a pure phenol amination. Observing the ratio of DCA and PhCHA formation over time reveals that within the first 6 h, both compounds are formed at a constant ratio of approx. 0.2, while this ratio gradually decreases thereafter (Fig. S 1). This indicates that the products are formed in parallel in the initial period, while DCA is slowly converted to phenylcyclohexylamine thereafter. Thus, cyclohexylamine is converted towards phenylcyclohexylamine, which is a net dehydrogenation, even if initially sodium formate was added. Further, dicyclohexylamine can be dehydrogenated towards the aromatic phenylcyclohexylamine, despite the initial presence of a reducing agent.

In a next step, the phenol amination with cyclohexylamine was investigated in the absence of sodium formate. The reaction of CHA

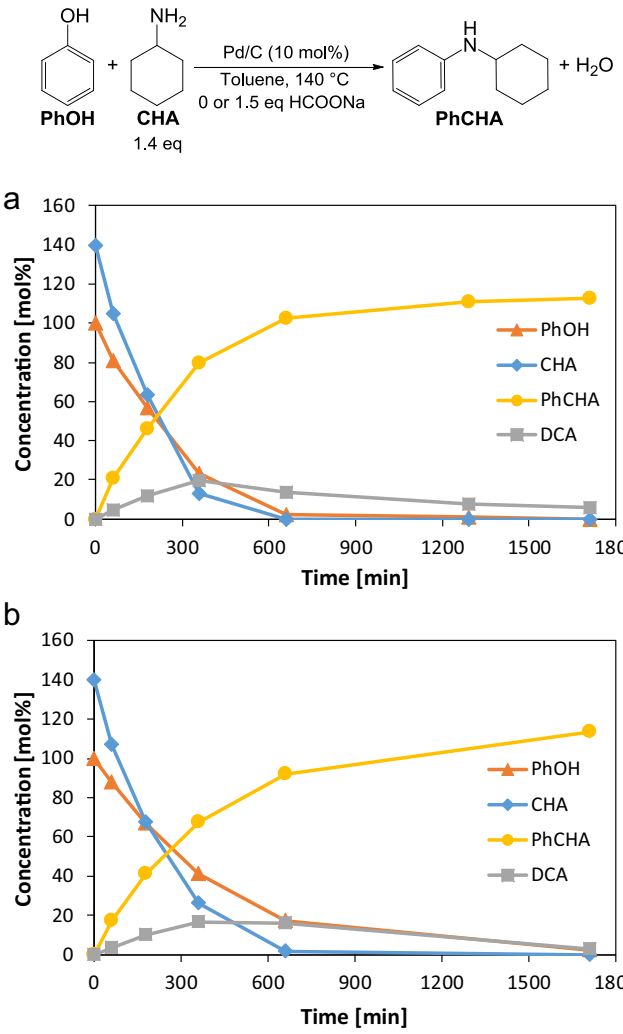
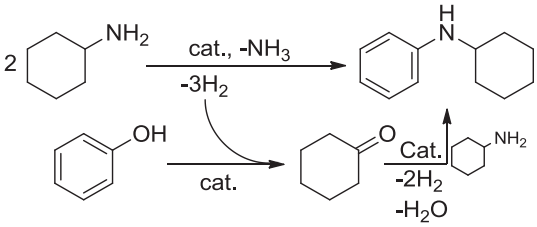


Fig. 1. Concentration-time diagram for the phenol (PhOH) amination using cyclohexylamine (CHA, 1.4 eq.) in the presence of sodium formate (a, 1.5 eq) and in the absence of sodium formate (b) towards *N*-phenylcyclohexylamine (PhCHA) and dicyclohexylamine (DCA) as side product. Reactions were carried out using Pd/C (10 mol%) and a 0.2 M solution of phenol at 140 °C.

towards PhCHA then should itself deliver the reducing equivalents to initiate the reaction of phenol to cyclohexanone (Scheme 3), which was observed in low amounts (<4 mol%). A reference reaction for the reaction of CHA in the absence of PhOH was carried out and the dehydrogenated PhCHA was observed as main product; the redox balance of this process proves that CHA makes reducing equivalents available (Fig. S 2). The concentration-time diagram for the amination of phenol using CHA in the absence of sodium formate (Fig. 1b) looks very similar to the previous one. However, the reaction takes place at a considerably lower rate. Also in this case, the concentration of PhCHA and DCA increased in an almost constant ratio in the first 6 h, while the concentration of DCA decreased thereafter and PhCHA is further produced (Fig. S 1). As for the reaction in the presence of sodium formate, the final concentration of PhCHA was 113 mol%.

The similarities between the reactions in the presence and absence of sodium formate are surprising. The similar time-concentration profiles indicate that the reactions proceed with the same general mechanism, just at different rates. However, the absence of sodium formate brings up a significant conceptual difference, which can be described as hydrogen borrowing: rather than an additional reductant being added, the initial reduction is driven by the amine serving as reductant. While in the most studied case of hydrogen borrowing, viz. aliphatic alcohol amination, the alcohol reactant is first dehydrogenated and then reacts with an amine, in the present reaction, it is the amine that reacts first, allowing for the reduction of the aromatic alcohol, hence the term 'reverse hydrogen borrowing.' This results in the formation of cyclohexylimine and the subsequent reaction towards PhCHA as a main product, and towards aniline, which is observed in low concentrations. This underlying mechanism also takes place in the presence of sodium formate, but less reducing capacity is present in the absence of sodium formate. Employing a larger amount of cyclohexylamine consequently increases the reducing capacity. To prove this concept, reactions in the presence of a higher amount of cyclohexylamine, i.e. 2.0 eq instead of 1.4 eq, were conducted in the presence and absence of sodium formate (Figs. S 3 and S 4). The overall reaction profiles look similar to those obtained in the prior experiments. PhCHA is formed in high yields with selectivities of >85% in both cases, with DCA as the only significant by-product. Most interesting, however, is the rate of phenol consumption (Fig. S 7). By increasing the amount of cyclohexylamine from 1.4 eq to 2 eq, the rate of reaction becomes equal to that of the reaction using 1.4 eq CHA and sodium formate. This shows how efficient the 'reverse hydrogen borrowing' strategy is, as 0.6 additional equivalents of amine have a similar effect as 1.5 eq sodium formate. Besides, the reaction in the presence of 2 eq amine and sodium formate shows the fastest progression, consistent with the proposed mechanism. A reference reaction using 4-methylphenol as substrate was performed to identify whether the cyclohexylamine reacts with the phenol (Figs. S 5, S 6). As expected, *N*-cyclohexyl-4-methylaniline was the main product formed from 4-methylphenol, albeit at a lower rate. This can be explained by lower reactivity of this substrate compared to phenol [16,17]. The final conversion of 4-methylphenol after 24 h was 64% in the presence and 59% in the absence of sodium formate, showing that reactivity is still similar. However, in the absence of sodium formate, more PhCHA is formed by condensation of cyclohexylamine.



Scheme 3. Concept of the amination of phenol without addition of a reductant using cyclohexylamine which can be transformed to phenylcyclohexylamine.

2.2. Amination of phenol with a non-cyclic aliphatic model amine

So far, the concept of direct amination of phenol without adding a reductant has been proven for cyclohexylamine. The products resulting from this reaction are interesting in themselves [18]. While cyclohexylamine is well suitable to assess activity and has strong reducing capabilities, an additional challenge is to expand the concept to different amines. Changing the amine might have two effects: (i) the amines may be less easily dehydrogenated, and (ii) side product formation might hinder product formation and decrease the selectivity. To investigate the effect of a different amine structure, 2-heptylamine was chosen, which can generate an imine upon dehydrogenation, corresponding to a maximum of two reducing equivalents per molecule of 2-heptylamine.

The conversion of phenol in the presence of sodium formate and 2-heptylamine proceeded more slowly than the amination in which cyclohexylamine is the amine (Fig. 2a). In contrast to the reaction with cyclohexylamine, there was a short induction period (1 h), in which phenol was not converted. After 6 h, 36% phenol was converted, compared to 77% in case of cyclohexylamine as amine. However, phenol was almost entirely converted after

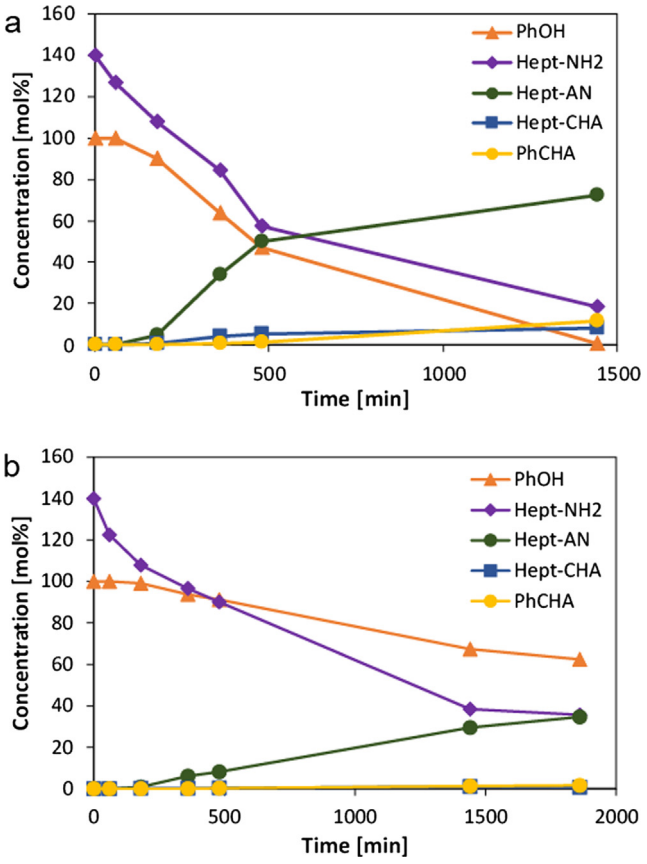


Fig. 2. Concentration-time diagram for the direct phenol amination using 2-heptylamine (Hept-NH_2, 1.4 eq.) in the presence (a) and absence (b) of sodium formate (1.5 eq). The products are *N*-(2-heptyl)aniline (Hept-AN), *N*-(2-heptyl)cyclohexylamine (Hept-CHA) and PhCHA. Reactions were carried out using Pd/C (10 mol%) and a 0.2 M solution of phenol at 140 °C.

24 h. Initially, 2-heptylamine is converted at a slightly higher rate than phenol, which is caused by the formation of condensation products, such as di(2-heptyl)amine and to a much lesser extent the corresponding imine. However, 2-heptylamine (Hept-NH_2) concentration was always higher than that of phenol; thus there should be no amine shortage throughout the reaction. *N*-(2-heptyl)aniline (Hept-AN) was formed as main product together with *N*-(2-heptyl)cyclohexylamine (Hept-CHA) in a ratio of approx. 8:1. The final yield of Hept-AN was 72%. Interestingly, a minor amount of Ph-CHA is formed with increasing phenol conversion. After 24 h a concentration of 11 mol% was reached, making it the most abundant side product. Cyclohexylamine is observed in trace amounts [19].

The reaction in the absence of sodium formate (Fig. 2b) also exhibits an induction period of at least 1 h in which no phenol is converted, and the reaction proceeds at a much lower rate. The final conversion after 24 h of reaction is 38%. 2-Heptylamine is converted at a similar rate as in the reaction in the presence of sodium formate for the first 3 h, although there is <1% phenol conversion; the main product during the initial phase of the reaction is the *N*-(2-heptyl)-2-heptylimine, which was detected by GC–MS. The product can be formed by condensation of 2-heptylimine with 2-heptylamine followed by elimination of ammonia [20]. Note that imines of primary amines are often rather unstable and could not be detected by GC-FID analysis; however small amounts of 2-heptanone were identified using GC–MS, showing that dehydrogenation of 2-heptylamine is possible. By dehydrogenation of the saturated amines (and eventual formation of the *N*-(2-heptyl)-2-heptylimine, cyclohexanone can be formed as intermediate. Thus, after 360 min of reaction, the formation of Hept-AN slowly proceeds with an almost constant rate to give a final yield of 35%. Remarkably, there is ≤1.5 mol% Hept-CHA and PhCHA formed. This results in a high Hept-AN selectivity of 92% with respect to the phenol consumed. A trimer of 2-heptylamine was identified by GC–MS with a final concentration of 9 mol% in the absence of sodium formate, while it is formed to a much lesser extent in the presence of sodium formate (≤1.5 mol%).

In summary, the amination of phenol using 2-heptylamine in the absence of a further reductant proceeds with excellent selectivity, but much more slowly and with a lower amination yield than in the reaction with sodium formate. This proves the feasibility of the approach of phenol amination without the addition of a reductant, but shows that the nature of the amine and, connected to this, the possibility to dehydrogenate the amine are significant factors in the reaction.

2.3. Amination of phenol with pyrrolidine

The first two examples showed that the dehydrogenation of the amine is significant. For this reason, pyrrolidine was chosen next, as its dehydrogenation is facile [21] and consequently it should provide high reactivity in the absence of an added reductant. Pyrrolidines have been employed for the formation of *N*-cyclohexylpyrroles from phenol, showing the intrinsic interest in this transformation [13]. The reaction has been carried out in the presence and in the absence of sodium formate (Fig. 3). Like for cyclohexylamine, there was no major difference in rate between the two reactions, besides from a slightly lower reactivity when no sodium formate is present. After 600 min phenol was fully (with sodium formate) or 97% converted (without sodium formate). However, pyrrolidine is readily dehydrogenated and is fully converted within the first 180 min towards either (partially) dehydrogenated pyrrolidines, i.e. pyrrolines and pyrrol, or the desired coupling products (Scheme 4). At complete pyrrolidine consumption, the cyclohexanone concentration increased up to 11 mol%. Initially, as long as pyrrolidine is present, its corresponding products *N*-phenylpyrrolidine (Ph-H_4Pyr) and *N*-cyclohexylpyrrolidine (Cy-H_4Pyr) are formed at a rather equal rate with a preference of approx. 19:1 over the fully dehydrogenated *N*-phenylpyrrolidine (Ph-Pyr), indicating clear preference for these products, as long as enough pyrrolidine is present. Thereafter, Cy-H_4Pyr is dehydrogenated to form the final products Ph-H_4Pyr and Ph-Pyr. Clearly, using the aromatic pyrrole, it is impossible to form the cyclohexyliminium salt, or the corresponding enamine. Further, in the absence of pyrrolidine there is a slight build-up in cyclohexanone concentration, which is caused by insufficient availability of pyrrolidine for the condensation reaction. Thus, pyrrole and partially

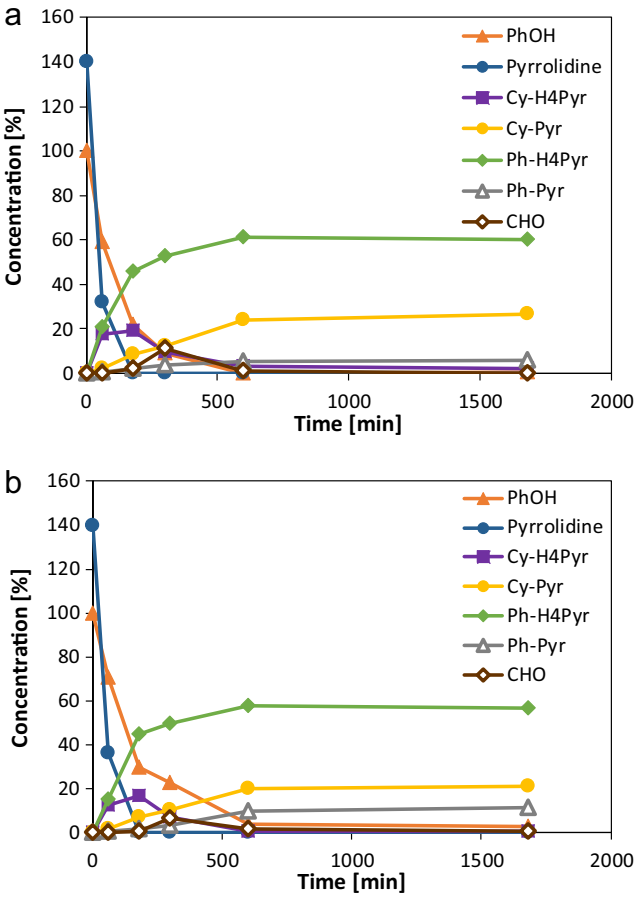
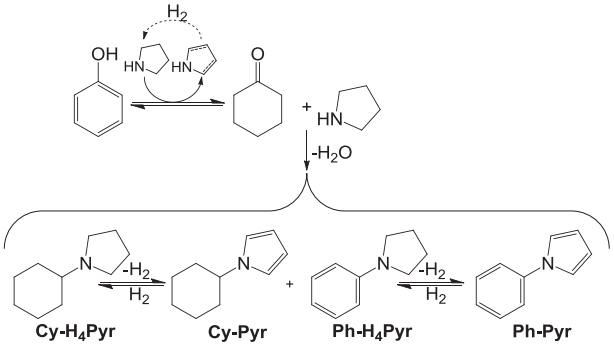


Fig. 3. Concentration-time diagram for the direct phenol amination using pyrrolidine (1.4 eq.) in the presence (a) and absence (b) of sodium formate (1.5 eq). The products are *N*-cyclohexylpyrrolidine (Cy-H4Pyr), *N*-cyclohexylpyrrole (Cy-Pyr), *N*-phenylpyrrolidine (Ph-H4Pyr) and *N*-phenylpyrrole (Ph-Pyr). Reactions were carried out using Pd/C (10 mol%) and a 0.2 M solution of phenol at 140 °C.



Scheme 4. Reaction sequence for the amination of phenol with pyrrolidine.

dehydrogenated pyrrolidine species must first be transformed back to pyrrolidine which readily reacts with cyclohexanone to form the final product.

These observations are valid, irrespective of the presence or absence of sodium formate. However, there are subtle differences between these two reactions, which can primarily be explained by the number of reducing equivalents available in the reaction mixture. After 10 h the amount of partially hydrogenated products slightly decreased, if no sodium formate is present: Ph-H_4Pyr decreased from 61 mol% to 57 mol% and the concentration of Cy-Pyr decreased from 24 mol% to 20 mol%. The completely dehydrogenated product Ph-Pyr is more abundant at the end of the reaction in the absence of sodium formate, with 11 mol%, than in its presence (6 mol%).

These results confirm that the amination of phenol without addition of a reductant can successfully proceed *via* an initial dehydrogenation of the amine. In this case, the dehydrogenated compounds derived from pyrrolidine are stable and they are formed readily. Thus, the reducing equivalents provided by pyrrolidine play a more important role than the reducing equivalents available from sodium formate, resulting in comparable rates for these two reactions.

2.4. Reaction of phenol with other N-heterocycles

In a next step, the reactivity of other heterocycles was investigated in the presence and absence of sodium formate (Table 1). Indoline (Table 1, Entry 1) is easily dehydrogenated to indole, corresponding to generation of two reducing equivalents. After 16 h of reaction, the reaction in the presence of 1.5 eq sodium formate yielded 54% of *N*-cyclohexylindole at a phenol conversion of 61%, while in the absence of sodium formate, 47% *N*-cyclohexylindole was formed at 49% phenol conversion. The higher conversion in the presence of sodium formate can easily be explained by more reducing equivalents being available. Note that the reaction in the absence of sodium formate provides exactly the maximum yield (47 mol%) possible using 1.4 eq (or 140 mol%) of indoline, taking into account that indoline dehydrogenation takes place, while the cyclohexyl group is hardly dehydrogenated:

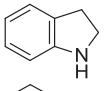
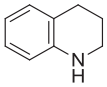
$$3\ \text{indoline} + \text{phenol} \rightarrow N\text{-cyclohexylindole} + 2\ \text{indole} + H_2O$$

This proves that indoline is an effective reductant in this conversion.

Next, piperidine was investigated for the reaction (Table 1, Entry 2). Each molecule of piperidine can be dehydrogenated yielding six reducing equivalents to form pyridine, which cannot react with cyclohexanone. In the presence of sodium formate, 92% of phenol was converted and the corresponding *N*-cyclohexyl and *N*-phenylpiperidine were formed in 55% and 24% yield, respectively. In the absence of sodium formate, 84% of phenol was converted and the corresponding *N*-cyclohexyl and *N*-phenylpiperidine were formed in 48% and 23% yield, respectively. Thus, the possibility of the amine to rather easily be dehydrogenated by aromatization to give six reducing equivalents explains the rather similar result between the reaction in the presence and absence of sodium formate. When 1,2,3,4-tetrahydroquinoline was used as amine (Table 1), cyclohexanone was observed as main product, which indicates that the condensation of this amine with cyclohexanone is sterically challenging. The yield of the corresponding substituted cyclohexylamine was 13% at 80% phenol conversion in the presence of sodium formate and only negligible amounts were formed at 39% conversion in the absence of sodium formate. The low extent of amination can be explained by the higher steric demand compared with the other amines. In the absence of an added reductant the amination is likely less pronounced, because there is a higher fraction of amine with a pyridine moiety (66% vs. 39%), which cannot form substituted amines. The degree of dehydrogenation is much lower than e.g. for pyrrolidine, which indicates that the dehydrogenation of 1,2,3,4-tetrahydroquinoline is rather challenging, explaining the larger difference in phenol conversion upon addition of sodium formate. Summarizing, the *N*-heterocycles that can rather easily be dehydrogenated induced higher rates in the conversion of phenol towards cyclohexanone and subsequent amination towards the aminated products.

To evaluate in a more quantitative way the reactivity induced by the different amine substrates, the phenol conversion was assessed after 3 h, and plotted as in Fig. 4. The horizontal axis gives the number of reducing equivalents, supposing full dehydrogenation of the amines, and full conversion of sodium formate to CO_2. The dehydrogenation of the amine does not necessarily result in the release of hydrogen gas; hydride species might as well be adsorbed on the catalyst surface where they are available for reducing the phenol. It has been demonstrated for the condensation and dehydrogenation of cyclohexylamine towards diphenylamine that H_2 gas may be accumulated in analogous conditions

Table 1
Amination of phenol with different *N*-heterocycles (1.4 eq.) in the presence and absence of sodium formate (1.5 eq) as reductant after 16 h of reaction. Reactions were carried out using Pd/C (10 mol%) and a 0.2 M solution of phenol at 140 °C.

Entry	Amine	Yield of cyclohexyl-/phenylamine (Phenol conversion)	
		With HCOONa	Without HCOONa
1		54[a]/- (61)	47[a]/- (49)
2		55/24 (92)	48/23 (84)
3		13/- (80)[b]	<1%/- (39)[b]

[a] The corresponding indole is formed as main product.
[b] Cyclohexanone was formed as main product.

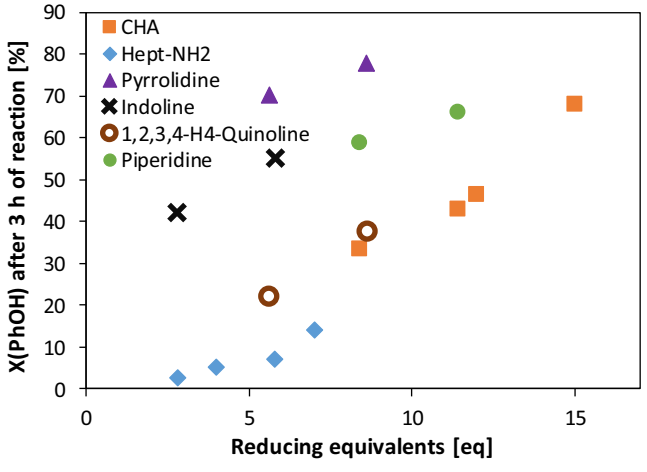


Fig. 4. Comparison of phenol conversion after 3 h in the presence of different amines. The number of reducing equivalents in the reaction mixture was calculated by summing the amount that would be available from either sodium formate (0 and 1.5 eq. with respect to the phenol) and from complete dehydrogenation of the amine to either the imine or the corresponding aromatic heterocycle. Reactions were carried out using Pd/C (10 mol%) and a 0.2 M solution of phenol at 140 °C.

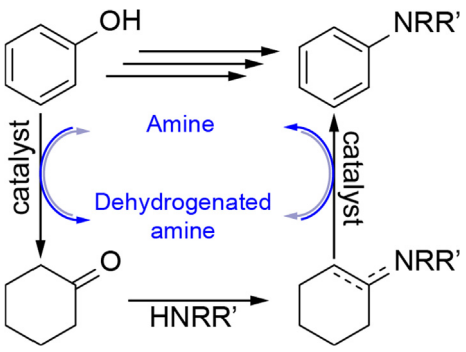
[18]. In the present reactions, it is likely that the available hydrogen is used to reduce organic acceptors, e.g. phenyl groups, since the catalyst is capable to install the equilibria between H_2 and the organic compounds. From Fig. 4, two general trends can be observed: (i) on the one hand, an increase in reducing equivalents results in a moderate increase in phenol conversion (for a given type of amine) and (ii) there is very different reactivity, depending on the type of amine. As seen before, 2-heptylamine is the least reactive of the investigated amines. Cyclohexylamine, which is rather easily condensed and dehydrogenated towards PhCHA, allows for higher reactivity than 2-heptylamine. However, when comparing similar levels of reducing equivalents, using pyrrolidine or piperidine as amine, it is obvious that a much higher conversion is obtained, which is based on the more easy dehydrogenation of these *N*-heterocycles. As reactions with and without sodium formate are represented in the graph, it is evident that the nature of the amine is more significant for the activity of the system than the amount of sodium formate added. Additionally a series of amines that cannot be dehydrogenated at all or only with difficulty, such as aniline or *tert*-butylamine, were tested (Table S 1); such reactions only resulted in low yields.

3. Conclusions

Prior studies focused on the amination of phenol in the presence of an extra added reducing agent, to form the corresponding *N*-substituted anilines or cyclohexylamines. Although different amines were employed in prior reports, there was so far no investigation regarding amine structure nor a reductant free reaction. Herein we present the phenol amination without addition of a reductant, in which, contrary to conventional hydrogen borrowing, the amine (rather than the alcohol) is first dehydrogenated to reduce phenol towards cyclohexanone, which can then react further (Scheme 5).

Distinct amines were investigated with respect to reactivity and selectivity to determine characteristics of the reaction network. The reactivity induced by the hydrogen borrowed from the amine heavily depends on how easily it can be dehydrogenated and how many reducing equivalents are available during dehydrogenation of the amine. If aromatic structures can be generated, as in the case of cyclohexylamine or piperidine, the reaction takes place at a similar rate, whether or not sodium formate is added. This is not the case when amines that are dehydrogenated less easily are used, such as 2-heptylamine. Further, the product distribution, more specifically the selectivity towards dehydrogenated products, is influenced by the presence of sodium formate, which generally promotes the formation of the corresponding cyclohexylamines.

It could be seen that the nature of the amine has a much higher impact on the reaction than the addition of sodium formate, showing that these results are significant for all reactions in the field of phenol amination *via* cyclohexanone. The reducing capabilities of the substituted amines are required to aid the amination. The here obtained results also suggest that various reductants can be used, given that they can be dehydrogenated using palladium, which might lead to new reactions in the future.



Scheme 5. Proposed concept for the amination of phenol without addition of a reductant.

4. Experimental section

All reactants were obtained from commercial suppliers and used as received. The Pd/C catalyst was obtained from Engelhard Corporation.

Reactions were performed in 10 mL crimp cap vials. If not stated otherwise, phenol (0.2 mmol), amine (1.4 eq, 0.28 mmol), Pd/C (5 wt% Pd, 10 mol% with respect to phenol) and toluene (1 mL) were added to the crimp cap vial which was closed and subsequently purged with nitrogen. The vials were placed in a metal block that was heated at 140 °C and the suspensions were stirred for 16 h. In case of kinetic experiments, the reaction was carried out in the same way, but the amounts were doubled. Small amounts of sample were taken at certain time intervals. All samples were filtered and subsequently analysed by GC-FID on a Shimadzu GC-2010 gas chromatograph equipped with an Agilent CP-Sil 5 CB column. All products were identified using GC–MS using an Agilent HP 6890 gas chromatograph and the peak area is correlated to the product using effective carbon numbers and normalizing to the initial phenol concentration [22]. The conversion was calculated as the amount of phenol converted and the yield of a compound was calculated as the percentage of the initial phenol concentration. The selectivity was obtained by dividing the yield by the conversion.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcat.2019.01.028.

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[19] Cyclohexylamine may be formed by reaction of an N-cyclohexylheptylimine with heptylamine or cyclohexanone with ammonia that is liberated during amine condensation. The intermediately formed cyclohexylamine can then react with an N-heptyl cyclohexylimine. Note that this reaction is simple, thus very low concentrations of both reactants are sufficient. The N heptyl cyclohexylimine can be formed by dehydrogenation of N-heptyl cyclohexylamine or hydrogenation of N-heptyl aniline. Thus, a significant amount of not fully dehydrogenated products is required to form PhCHA as significant by-product.
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