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Rhenium-catalyzed amination of alcohols by hydrogen transfer process

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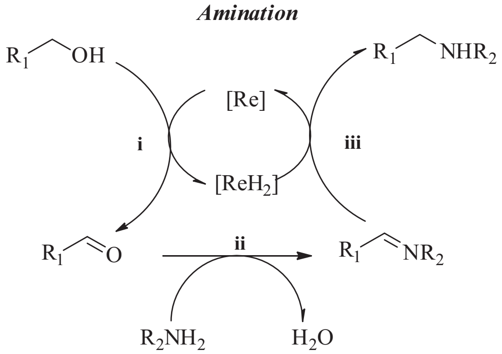
ABSTRACT

The rhenium heptahydride complex [$ReH_7(PCy_3)_2$] was found to be an effective homogeneous catalyst for amination of various alcohols through hydrogen transfer mechanism. Under carbon monoxide atmosphere, a variety of primary and secondary alcohols could directly undergo the C—N coupling process.

Introduction

The nitrogen-containing compounds are of great importance owing to their diverse biological activities, and thus the development of efficient methods to construct C—N bonds has emerged as a major task in organic synthesis.[1] Copper-catalyzed Ullmann and Goldberg couplings,[2] as well as palladium-catalyzed Buchwald–Hartwig aminations[3] with haloarenes have been widely accepted as the most efficient methods to construct C—N bonds. The amination of alcohols through a hydrogen transfer process is also a powerful tool for direct construction of C—N bond.[4] Compared with alkyl halides, alcohols are much more favored in terms of their simplicity of operation and storage. In those transformations, most of them could be catalyzed by Ir[5] or Ru.[6] Catalysts derived from other metals, such as Au, Ni, Pd, and Rh, have also been explored.[7] However, it is still desirable to develop a new catalyst for this transformation.

In past decades, Re was widely applied to organic synthesis.[8] As our on-going interests in Re-complex-catalyzed hydrogen transfer process,[9] we are interested in the development of an amination protocol of amines with alcohols by hydrogen transfer reaction featuring the only waste to be the water generated in the reaction (Scheme 1).



Scheme 1. Rhenium-catalyzed dehydrogenative C—C coupling via dual activation model.

Results and discussion

In our initial study, the reaction of aniline **1a** and 1-phenylethanol **2a** was chosen as the model reaction. The results are summarized in Table 1. Treatment of the reaction under Ar, air or H_2 atmosphere in the catalysis of $ReH_7(PCy_3)_2$ (PCy_3 = tricyclohexylphosphine) did not give any desired product (Table 1, entries 1–3). To our delight, when the amination reaction was run under CO atmosphere with the same catalyst, **3a** was obtained in 80% yield (Table 1, entry 4). Other rhenium heptahydride complexes

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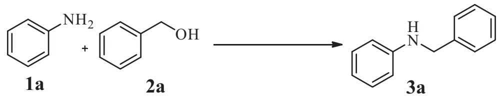
Table 1
The optimization of reaction conditions for amination

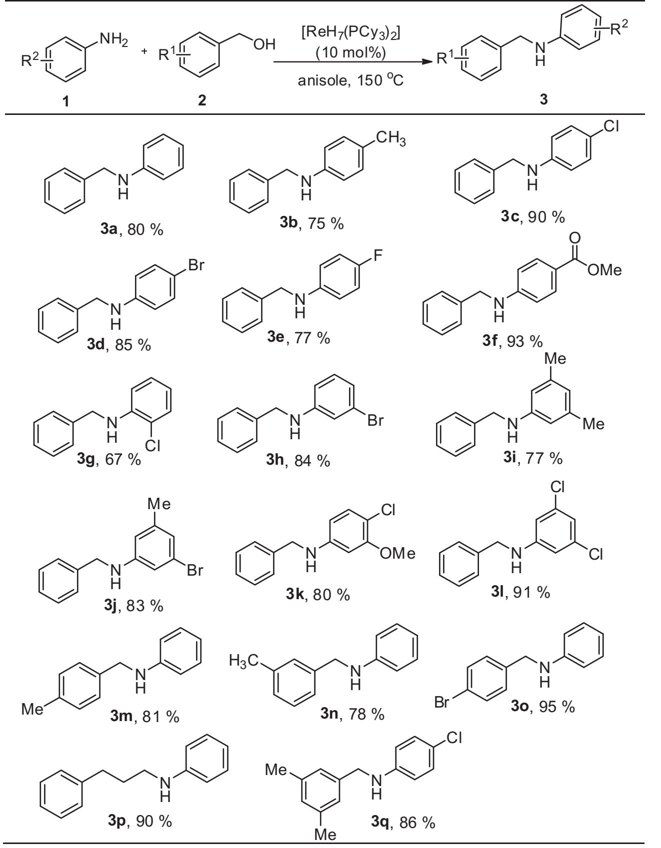


Entry	Re complex	Atmosphere	Solvent	Additive	Yield[a]
1	$ReH_7(PCy_3)_2$	Ar	Anisole		0
2	$ReH_7(PCy_3)_2$	Air	Anisole		0
3	$ReH_7(PCy_3)_2$	H_2	Anisole		0
4	$ReH_7(PCy_3)_2$	CO	Anisole		80
5	$ReH_7(PPh_3)_2$	CO	Anisole		30
6	ReH_7(dppe)	CO	Anisole		0
7	ReH_7(dppf)	CO	Anisole		0
8	$ReH_7(PCy_3)_2$	CO	THF		42
9	$ReH_7(PCy_3)_2$	CO	DMF		48
10	$ReH_7(PCy_3)_2$	CO	Toluene		50
11	$ReH_7(PCy_3)_2$	CO	DCM		40
12	$ReH_7(PCy_3)_2$	CO	Chlorobenzene		40
13	$ReH_7(PCy_3)_2$	CO	CH_3CN		0
14	$ReH_7(PCy_3)_2$	CO	Anisole	LiCl	51
15	$ReH_7(PCy_3)_2$	CO	Anisole	4 Å MS	67
16	$ReH_7(PCy_3)_2$	CO	Anisole	$MgBr_2$	46
17	$ReH_7(PCy_3)_2$	CO	Anisole	$MgSO_4$	50

[a] Reaction conditions: **1a** (1.2 mmol), **2a** (0.4 mmol), Re complex (10 mol %), solvent (0.5 mL), CO atmosphere (1.5 atm), 150 °C. Isolated yield.

were also examined, but the results were not satisfactory (Table 1, entries 5–7). From screening of various solvents and additives, it was found that the Re-catalyzed amination reaction could not be improved more efficiently (Table 1, entries 8–18). Consequently, the optimal reaction conditions should include the catalysis by 10 mol % $ReH_7(PCy_3)_2$ at 150 °C under CO atmosphere (1.5 atm) with anisole as the solvent (Table 1, entry 4).

Table 2
Scope of the reaction for the synthesis of indolequinones[a]



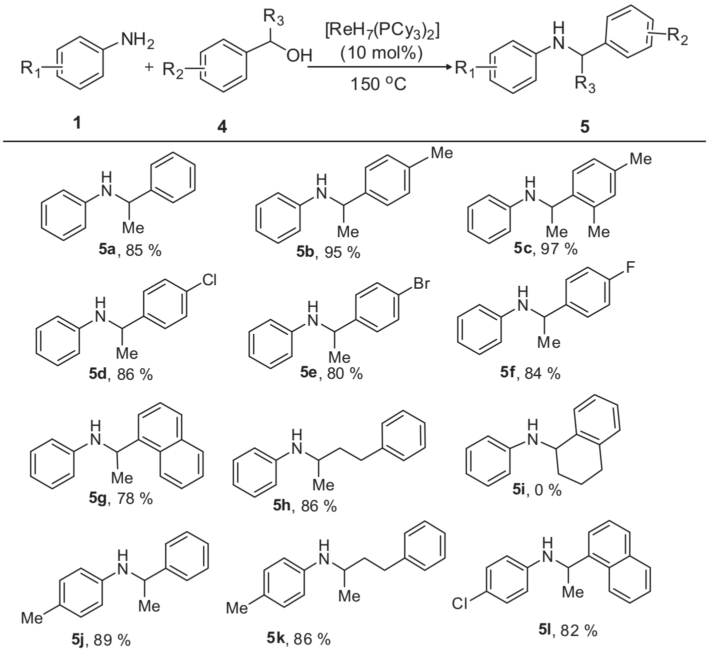
[a] Reaction conditions: **1a** (1.2 mmol), **2a** (0.4 mmol), $ReH_7(PCy_3)_2$ (10 mol %), anisole (0.5 mL), CO atmosphere (1.5 atm), 150 °C. Isolated yield.

With the optimized reaction conditions established, we investigated the reaction scope of this protocol. We investigated that if the primary alcohols are employed, the corresponding aldehydes are able to react with anilines readily followed by reduction through hydrogen transfer process. In this way, we subsequently tested the amination protocol with primary alcohols. The results are summarized in Table 2. To our delight, it was found that a wider range of anilines could run the *N*-benzyl reaction smoothly to afford the expected products **3a**–**l** in good to excellent yields. The anilines bearing electron-deficient and electron-rich functional groups in either *meta* or *para* positions were effective under the optimal reaction conditions. When 2-chloroaniline was subjected to the reaction conditions, moderate yield (**3g**, 67%) was obtained owing to its steric hindrance of chlorine atom. Pleasingly, other substituted primary alcohols were able to be alkylating reagent in our protocol. The desired products **3m**–**q** could be obtained in 78–95% yields. It is important to point out that the reaction has good selectivity, and only the mono amination products are observed.

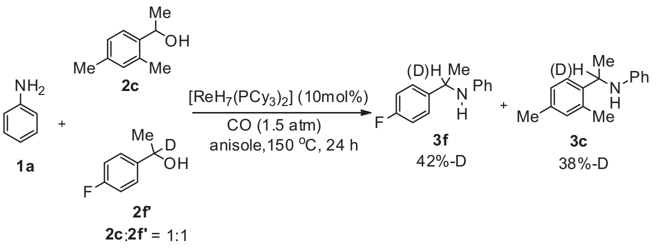
Subsequently, different secondary alcohols were examined (Table 3). It was found that benzyl alcohols bearing electron-donating substituents on the aromatic rings could perform the reaction smoothly to provide the amination products **5a**–**c** in 85–97% yields. Satisfactory yields were obtained when the benzyl alcohols involving a halide substitution (**5d**–**f**), and no dehalogenation products were detected. To our surprise, when 1,2,3,4-tetrahydronaphthalen-2-ol was subjected to the standard reaction conditions, no desired product **5i** could be formed mainly owing to the relatively inert character of the generated cycloketone. Besides the benzylic alcohols, the simple aliphatic alcohols were also effective to generate the amination products (**5h** and **5k**) in moderated yields.

To gain insight into the mechanistic pathway of Re-catalyzed amination reaction, a H/D exchanging experiment was carried out. When aniline **1a** was reacted with a mixture of benzylic

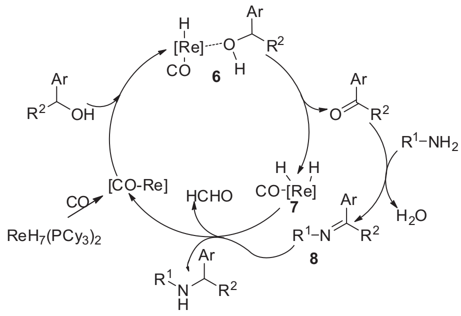
Table 3
Scope of the reaction for the synthesis of polysubstituted pyrroles[a]



[a] Reaction conditions: **1a** (1.2 mmol), **4** (0.4 mmol), $ReH_7(PCy_3)_2$ (10 mol %), anisole (0.5 mL), CO atmosphere (1.5 atm), 150 °C. Isolated yield.



Scheme 2. Deuteration experiments.



Scheme 3. Proposed mechanism.

alcohols **2c** and **2f**′ under CO atmosphere at 150 °C for 24 h, it was found that 42% D was observed in product **3f** and 38%-D was observed in product **3c** (Scheme 2). This may suggest the alcohol hydrogen transfer process. Based on our previous work,[9] it was found that the coordination of anilines to rhenium could lead to catalyst deactivation. Thus, CO was introduced to stabilize the active rhenium species.

At present, the proposed mechanism is shown in Scheme 3. Firstly, $ReH_7(PCy_3)_2$ decomposed into a rhenium carbonyl complex via CO coordination. Then, coordination of the O atom of alcohol to Re generates the intermediate **6**. Subsequently, the corresponding aldehyde or ketone is generated in situ from **6** through further loss of hydrogen. Then, imine **8** could be formed under from carbonyl compound and amine. Finally, reduction of imine **8** with [Re-H_2] species **7** produces the desired product and completes the catalytic cycle.

Conclusions

In summary, we have developed a Re-catalyzed amination protocol of primary and secondary alcohols. A variety of anilines are able to convert to the corresponding secondary amines with a range of benzyl alcohols in good to excellent yields, and no over-alkylated products could be detected. Furthermore, the only waste generated through the overall process is water. In addition, it is a new development in the field of rhenium chemistry.

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Supplementary data

Supplementary data (experimental details and the characterization data) associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2014.05.068.

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