Pergamon

Tetrahedron Letters 39 (1998) 1017–1020

TETRAHEDRON LETTERS

# Reduction of Amides to Amines via Catalytic Hydrosilylation by a Rhodium Complex

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Received 7 November 1997; revised 4 December 1997; accepted 5 December 1997

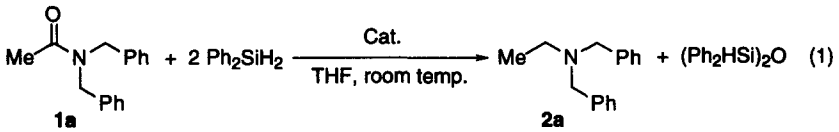
***Abstract:*** Reduction of a wide range of tertiary amides with 2 molar equivalents of diphenylsilane was promoted by 0.1 mol% of $RhH(CO)(PPh_3)_3$ at room temperature, affording the corresponding tertiary amines in high yields. The synthetic utility is demonstrated by chemoselective reductions of amides having functional groups such as ester and epoxy groups which are not tolerated by the conventional reductions with $LiAlH_4$ and $BH_3$. 

The synthetic usefulness of hydrosilylation has been demonstrated in the stereoselective and chemoselective reduction of carbonyl groups.[1] The hydrosilylations of aldehydes, ketones,[2] and esters[3] are catalyzed by some transition metal complexes. In general, carboxamides have been reluctant to the reduction with hydrosilanes, although it is reported that $Cl_3SiH$ with tripropylamine is capable of reducing aromatic tertiary amides to amines.[4,5] Herein, we wish to describe that a rhodium complex catalyzed reaction of various tertiary carboxamides with a hydrosilane, giving the corresponding amines in high yields. Some chemoselectivities of the present reduction, which are not accessible with $LiAlH_4$ and $BH_3$, provide utility in organic synthesis of tertiary amines.

Reaction of *N,N*-dibenzylacetamide (**1a**) with a hydrosilane was examined by a catalytic amount of some rhodium compounds (eq. 1), as summarized in Table 1. The reaction with 2.1 molar equivalents of $Ph_2SiH_2$ in the presence of 0.1 mol% of $RhH(CO)(PPh_3)_3$ completed within 1 h at room temperature, and yielded dibenzylethylamine (**2a**) and $(Ph_2HSi)_2O$ (entry 1). The high turnover frequency with $RhH(PPh_3)_4$ is also noted (entry 2). Other rhodium complexes without a hydride ligand, $[Rh(COD)_2]BF_4$–$2PPh_3$, $RhCl(PPh_3)_3$ and $RhCl_3{\cdot}3H_2O$, could promote the reduction of **1a** to afford **2a** in high yields, but these reactions proceeded sluggishly under similar conditions (entries 3–5). Use of 1.0 molar equivalent of $Ph_2SiH_2$ for the reduction of **1a** gave **2a** in 49% isolated yield with 50% of the starting material (entry 6). The hydride on $(Ph_2HSi)_2O$ did not participate in the reduction. Reaction of **1a** with 1.1 molar equivalent of $PhSiH_3$ gave **2a** in 90% yield together with polysiloxane $(PhHSiO)_n$ (entry 7). Monohydrosilane, $Ph_3SiH$, did not react with **1a** in the presence of the rhodium catalyst (entry 8).

0040-4039/98/$19.00 
*PII:* S0040-4039(97)10804-8

**Table 1.** Rhodium-Catalyzed Reduction of *N,N*-Dibenzylacetamide (**1a**) to **2a** with Hydrosilane.[a]




**1a** **2a**

| Entry | Catalyst | Hydrosilane | Time, h | Yield (**2a**), %[b] |
|---|---|---|---|---|
| 1 | $RhH(CO)(PPh_3)_3$ | $Ph_2SiH_2$ | 1 | 94 |
| 2 | $RhH(PPh_3)_4$ | $Ph_2SiH_2$ | 0.5 | 93 |
| 3 | $[Rh(COD)_2]BF_4 - 2PPh_3$ | $Ph_2SiH_2$ | 42 | 86 |
| 4 | $RhCl(PPh_3)_3$ | $Ph_2SiH_2$ | 48 | 93 |
| 5 | $RhCl_3 \cdot 3H_2O$ | $Ph_2SiH_2$ | 48 | 95 |
| 6 | $RhH(CO)(PPh_3)_3$ | $Ph_2SiH_2$[c] | 1 | 49 |
| 7 | $RhH(CO)(PPh_3)_3$ | $PhSiH_3$[d] | 2 | 90 |
| 8 | $RhH(CO)(PPh_3)_3$ | $Ph_3SiH$ | No Reaction | |

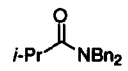
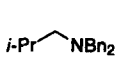
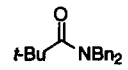
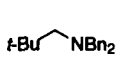
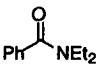
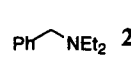
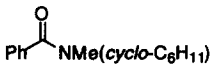
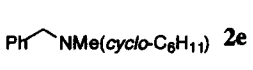
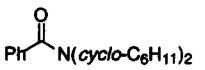
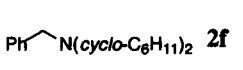
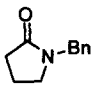
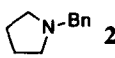
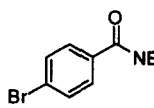
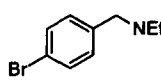
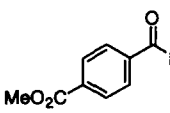
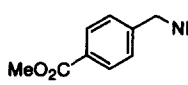
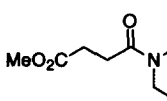
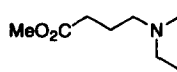
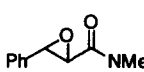
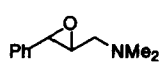
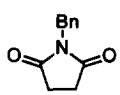
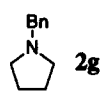
[a] Reactions were carried out in THF (1 ml) at room temperature. The ratio of **1a** (1 mmol):hydrosilane:catalyst was 1000:2100:1 unless otherwise noted. [b] Isolated yield. [c] 1.0 molar equivalent of $Ph_2SiH_2$ was used. [d] 1.1 molar equivalent of $PhSiH_3$ was used.

To explore the scope of the catalytic reaction, the reduction of a wide range of amides was investigated (Table 2). The reaction rate was considerably affected by steric bulkiness of the substituents on the carbonyl carbon as well as on the nitrogen atom, although the reactions of sterically bulky amides gave the corresponding amines in high yields (entries 1–5). Benzamide **1d** was easily reduced with $Ph_2SiH_2$ at room temperature in 2 h to give **2d** in 86% yield, regardless of the bulkiness of the acyl substituent. Lactam **1g** was also converted into **2g** in good yield (entry 6). Some functional groups intolerable for $LiAlH_4$ and/or $BH_3$ survived the reduction with $Ph_2SiH_2$ in the presence of the rhodium complex. Amide substrates **1h–k** bearing a bromo, ester or epoxy group were converted chemoselectively to the corresponding amines **2h–k** (entries 7–10).[6] However, the reduction of the amides having C–C double and triple bonds, and α-active methylene gave complicated mixtures. No primary and secondary amides reacted with hydrosilane in the presence of $RhH(CO)(PPh_3)_3$. Reduction of imide **1l** with 4 molar equivalents of $Ph_2SiH_2$ resulted in selective formation of the corresponding cyclic amine **2g** (entry 11).

Typical procedure for the reduction of amides to amines is presented as follows. To a mixture of amide **1** (1.0 mmol) and 0.1 mol% of $RhH(CO)(PPh_3)_3$ in THF (1 ml) or without a solvent was added 2.1–2.5 molar equivalents of $Ph_2SiH_2$ at room temperature. After completion of the reaction, the mixture was diluted with $Et_2O$, and extracted with 1 N HCl aq. The aqueous layer was basified with 15% NaOH aq and extracted with AcOEt. The organic layer was dried over $Na_2SO_4$ and concentrated under reduced pressure to give the corresponding amine **2**, which is almost pure.

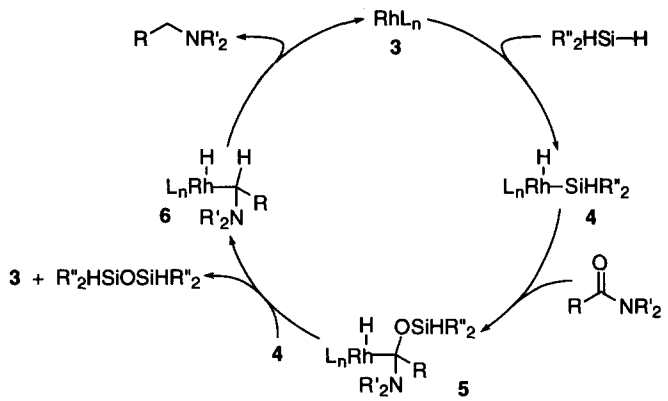
Although the mechanism for the present reduction of amides with a hydrosilane remains to be investigated, the catalytic cycle may start from oxidative addition of hydrosilane to Rh(I) complex (**3**), forming hydrido(silyl)rhodium(III) (**4**), whose Rh–Si bond undergoes insertion of an amide carbonyl group. It might be presumed that rapid hydride transfer to the resultant Rh(III) complex (**5**) from **4** leads to selective reductive

**Table 2.** $RhH(CO)(PPh_3)_3$-Catalyzed Reduction of Amides (**1**) to Amines (**2**) with $Ph_2SiH_2$.[a]

| Entry | Amide (**1**) | Time, h | Product (**2**) | Yield, %[b] |
|---|---|---|---|---|
| 1 |  **1b** | 24 |  **2b** | 90 |
| 2[c] |  **1c** | 48 |  **2c** | 86 |
| 3 |  **1d** | 2 |  **2d** | 85 |
| 4 |  **1e** | 4 |  **2e** | 91 |
| 5 |  **1f** | 48 |  **2f** | 83 |
| 6 |  **1g** | 0.5 |  **2g** | 66 |
| 7 |  **1h** | 20 |  **2h** | 85 |
| 8 |  **1i** | 4.5 |  **2i** | 70 |
| 9[d] |  **1j** | 3 |  **2j** | 98[e] |
| 10[d] |  **1k** | 3 |  **2k** | 65 |
| 11[f] |  **1l** | 3.5 |  **2g** | 70 |

[a] Reactions were carried out in THF (1 ml) at room temperature. The ratio of **1** (1 mmol):$Ph_2SiH_2$:$RhH(CO)(PPh_3)_3$ was 1000:2100:1 unless otherwise noted. [b] Isolated yield unless otherwise noted. [c] The reaction was carried out with 2.5 molar equivalents of $Ph_2SiH_2$ without solvent. [d] 1 mol% of $RhH(CO)(PPh_3)_3$ was used. [e] GLC yield. [f] 4.3 molar equivalents of $Ph_2SiH_2$ were used.

**Scheme 1**




cleavage of the C–O bond of **5** with the formation of alkylrhodium complex **6**.[7] The catalytic cycle ends up with reductive elimination from **6**.

In summary, we have developed an efficient method for the reduction of amides to amines which proceeds under mild conditions and gives almost pure products with only extractive workup. The reaction may be useful for chemoselective reduction of amides bearing functional groups intolerable for $LiAlH_4$ and/or $BH_3$. Further studies are under way to improve the chemoselectivity of the present catalytic reaction.

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