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Communications

Nickel-Catalyzed Reduction of Aromatic Ring of Phenanthrolines

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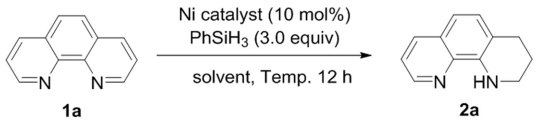
Reduction reactions represent a cornerstone of organic synthesis, pivotal in the diverse landscape of chemical transformations. Among these, the reduction of unsaturated aromatic compounds to their saturated counterparts stands as a critical and versatile process, offering the potential to convert aromatic substrates into valuable derivatives with myriad applications in chemistry and industry.[1] The realm of nitrogen-containing heterocyclic aromatic compounds, in particular, has garnered significant attention from researchers seeking innovative methods for reduction.[2]

Recent strides in the field have witnessed the emergence of transition metal complexes as powerful tools in catalytic reductions. Notable metals such as rhodium,[3] ruthenium,[4] palladium,[5] iridium,[6] iron,[7] and cobalt[8] have been harnessed for their catalytic prowess, often coupled with silane compounds as efficient hydride donors. These advancements have enriched our toolbox for the controlled reduction of aromatic structures.

Curiously, despite the remarkable progress in this arena, a nickel-catalyzed synthesis of nitrogen-containing heterocyclic aromatic compounds through reduction remains conspicuously absent in the literature. In response to this uncharted territory, we embarked on a systematic study aimed at pioneering a novel nickel-catalyzed reduction method.

Our investigation centers on the utilization of phenanthroline as a model substrate, serving as a robust platform to elucidate the reactivity and efficacy of diverse nickel catalyst species in concert with the hydride donor $PhSiH_3$.[9] The results are summarized in *Table* 1. Our experimentation reveals that when $Ni(OAc)_2{\cdot}4H_2O$ assumes the role of catalyst, CH_3CN as the solvent, and the reaction is conducted at a temperature of 40 ℃, the desired product **2a** is obtained in an impressive 89% yield (entry 1). Encouragingly, similar outcomes are achieved when alternative nickel catalysts such as $NiCl_2$, $Ni(acac)_2$, $Ni(OTf)_2$, and $NiCl_2$(glyme) are employed (entries 2–5). However, it is noteworthy that the yields with these catalysts are marginally lower compared to the reaction employing $Ni(OAc)_2$. Furthermore, our investigation highlights the significant influence of solvent choice on reaction outcomes. Employing DMSO (dimethyl sulfoxide) and DMF (N,N-dimethyl formamide) as alternative solvents yields products in high yields of 86% and 85%, respectively (entries 6 and 7). In contrast, the use of $ClCH_2CH_2Cl$ and H_2O results in comparatively lower yields of 41% and 31% (entries 8 and 9). Notably, commonly employed solvents like THF and toluene prove ineffective, failing to produce any discernible

***Table* 1.** Optimization of nickel-catalyzed reduction of phenanthroline[a]

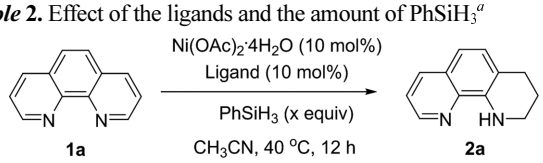


1a **2a**

Entry	Catalyst	solvent	Temp (℃)	Yield (%)[b]
1	$Ni(OAc)_2{\cdot}4H_2O$	CH_3CN	40	89 (89)[c]
2	$NiCl_2$	CH_3CN	40	62
3	$Ni(acac)_2$	CH_3CN	40	67
4	$Ni(OTf)_2$	CH_3CN	40	81
5	$NiCl_2$(glyme)	CH_3CN	40	80
6	$Ni(OAc)_2{\cdot}4H_2O$	DMSO	40	86
7	$Ni(OAc)_2{\cdot}4H_2O$	DMF	40	85
8	$Ni(OAc)_2{\cdot}4H_2O$	$ClCH_2CH_2Cl$	40	41
9	$Ni(OAc)_2{\cdot}4H_2O$	H_2O	40	31
10	$Ni(OAc)_2{\cdot}4H_2O$	THF	40	0
11	$Ni(OAc)_2{\cdot}4H_2O$	toluene	40	0
12	$Ni(OAc)_2{\cdot}4H_2O$	CH_3CN	25	43
13	$Ni(OAc)_2{\cdot}4H_2O$	CH_3CN	80	88

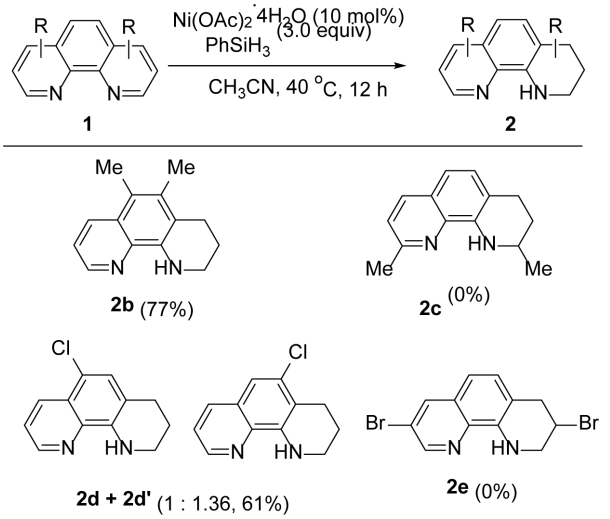
[a]Reaction conditions: **1a** (0.3 mmol), Ni catalyst (0.03 mmol), and $PhSiH_3$ (0.9 mmol) reacted in solvent (1.0 mL) for 12 h. [b]Determined by gas chromatography with an internal standard. [c]Isolated yield using 2.0 mmol scale.

***Table* 2.** Effect of the ligands and the amount of $PhSiH_3$[a]



Entry	Ligand	$PhSiH_3$ (x equiv)	Yield (%)[b]
1	TMEDA	3.0	82
2	2,2'-Bipyridine	3.0	83
3	4,4'-di-tert-butyl-2,2'-bipyridine	3.0	88
4	4,4'-dimethoxy-2,2'-bipyridine	3.0	88
5	-	5.0	89
6	-	10.0	89

[a]Reaction conditions: **1a** (0.3 mmol), $Ni(OAc)_2.4H_2O$ catalyst (0.03 mmol), ligand (0.03 mmol) and $PhSiH_3$ reacted in CH_3CN (1.0 mL) for 12 h. [b]Determined by gas chromatography with an internal standard.



***Scheme* 1.** Reduction of phenanthroline derivatives.

products (entries 10 and 11). No product was obtained when the reaction was allowed to run for 24 h or at 80 ℃ in THF and toluene. Additionally, we observe that a reduction in reaction temperature to 25 ℃ affords a 43% reaction yield, while elevating the temperature to 80 ℃ does not lead to a significant improvement, yielding results analogous to the 40 ℃ condition (entries 12 and 13).

Additional experiments were conducted to augment the reaction yield. The outcomes are succinctly presented in *Table* 2. When TMEDA served as the ligand, the reaction yield experienced a marginal decrease to 82%, and with the use of 2,2'-bipyridine, the yield also exhibited a slight reduction to 83% (entries 1 and 2). Employing 4,4'-di-tert-butyl-2,2'-bipyridine and 4,4'-dimethoxy-2,2'-bipyridine as ligands yielded 88%, a comparable result to the reaction conducted without ligands (entries 3 and 4). Augmenting the amount of PhSiH3 to 5 and 10 equivalents did not yield an increase in the reaction yield (entries 5 and 6).

Through rigorous exploration of reaction conditions, we have successfully established optimized parameters. The ideal conditions encompass the use of a 10 mol% nickel catalyst, 3 equivalents of $PhSiH_3$, and CH_3CN as the solvent. Under these conditions, the reaction proceeds efficiently for 24 hours at 40 ℃. Encouraged by this success, we extended our investigation to include substituted phenanthroline derivatives, and the results are thoughtfully summarized in *Scheme* 1. We found that 4,5-dimethyl-substituted phenanthroline gave the desired product **2b** in 77% yield, however, 2,9-dimehtyl-substituted phenanthroline did not give the reduced product. When 5-chloro-1,10-phenanthroline was employed, the mixture of 5-chloro-1,2,3,4-tetrahydro-phenanthroline and 6-chloro-1,2,3,4-tetrahydro-phenanthroline (**2d** + **2d'**, ratio **2d/2d'** = 1: 1.36) was formed in 61% yield. Unfortunately, 3,8-dibromo-1,10-phenanthroline did not produce the reduced product **2e**.

The culmination of our research signifies a pioneering achievement—the inaugural nickel-catalyzed synthesis of nitrogen-containing heterocyclic aromatic compounds through a partial reduction strategy. Employing $Ni(OAc)_2·4H_2O$ as the catalyst and $PhSiH_3$ as the hydride source, we have demonstrated that the reaction proceeds smoothly at 40 ℃ in CH_3CN, consistently delivering the desired compounds in good yields.

Experimental Section

General Information

All reagents employed in this study were sourced and utilized without further purification. Nuclear Magnetic Resonance (NMR) spectra, including ^1H and ^{13}C NMR, were meticulously recorded in $CDCl_3$ on high-field spectrometers. NMR data is comprehensively reported, encompassing chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constants (Hz), and integration.

General Experimental Method

The experimental procedure entailed the meticulous combination of phenanthroline derivatives (2.0 mmol), $Ni(OAc)_2·4H_2O$ (49.6 mg, 0.2 mmol), and PhSiH3 (648 mg, 6.0 mmol) within a 20 mL vial. This reaction mixture was subsequently treated with CH_3CN (10.0 mL) and stirred

diligently at a controlled temperature of 40 ℃ for a duration of 12 hours. Upon the completion of the reaction, EtOAc (20.0 mL) was introduced to the mixture, followed by the addition of NH_4Cl aqueous solution (25 mL). A meticulous separation of the organic solvent layer was facilitated, subsequently augmenting it with an aqueous solution of $NaHCO_3$ (25 mL) before subjecting it to filtration post-treatment with $MgSO_4$. Subsequent removal of solvent from the organic layer was achieved through evaporation, with the final compound being isolated meticulously using column chromatography, employing a silica gel-packed column.

Reduction of 1a[10]

According to general procedure, phenanthroline (360 mg, 2.0 mmol) afforded **2a** (328 mg, 1.78 mmol, 89%). ^{1}H NMR 8.69 (m, 1H), 8.01 (dd, J = 8.4, 1.8 Hz, 1H), 7.28 (dd, J = 7.8, 4.2 Hz, 1H), 7.17 (d, J = 8.4 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 5.94 (s, 1H), 3.53 (m, 2H), 2.92 (m, 2H), 2.06 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$); 146.9, 140.7, 137.5, 135.9, 129.1, 127.4, 120.5, 116.5, 113.1, 41.3, 27.0, 21.8.

Reduction of 1b[10]

According to general procedure, 5,6-dimethyl-1,10-phenantrhroline (416 mg, 2.0 mmol) afforded 2c (326 mg, 1.54 mmol, 77%), ^{1}H NMR (400 MHz, $CDCl_3$) 8.65 (d, J = 4.2 Hz, 1H), 8.24 (d, J = 8.6 Hz, 1H), 7.32 (dd, J = 8.6, 4.1 Hz, 1H), 5.95 (br s, 1H), 3.46 (m, 2H), 2.83 (t, J = 6.5 Hz, 2H), 2.49 (s, 3H), 2.33 (s, 3H), 2.11 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$), 145.7, 139.0, 136.8, 134.2, 132.1, 126.2, 120.3, 117.0, 116.7, 40.7, 25.2, 22.7, 15.9, 13.7.

Reduction of 1d

According to general procedure, 2,9-dimethyl-1,10-phenantrhroline (416 mg, 2.0 mmol) afforded **2d** + **2d'** (266 mg, 1.22 mmol, 61%), ^{1}H NMR (400 MHz, $CDCl_3$) 8.70 (m, 0.4H), 8.64 (m, 0.6H), 8.40 (m, 0.4H), 7.91 (m, 0.6H), 7.41 (m, 0.4H), 7.40 (m, 0.6H)7.23 (s, 0.4H), 7.1 (s, 0.6H), 6.19 (br s, 0.6H), 5.97 (br s, 0.4H), 3.50 (m, 2H), 2.95-2.87 (m, 2H), 2.10-2.03 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$), 147.2 (M), 146.8 (m), 142.4 (M), 140.1 (m), 137.8 (M), 135.9 (m), 135.0 (M), 134.5 (m), 132.8 (m), 128.7 (M), 127.4 (M), 125.0 (m), 121.5 (M), 121.2 (m), 116.5 (M), 115.3 (m), 114.3 (m), 112.0 (M), 41.1 (m), 40.5 (M), 25.9 (m), 24.8 (M), 21.6 (m), 21.5(M) (M = major peak, m = minor peak). HRMS (FD-TOF) m/z: $[M]^+$ Calcd for $C_{12}H_{11}N_2Cl$ 218.06053; Found 218.06032.

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Supporting Information. Spectral data for the products.

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