

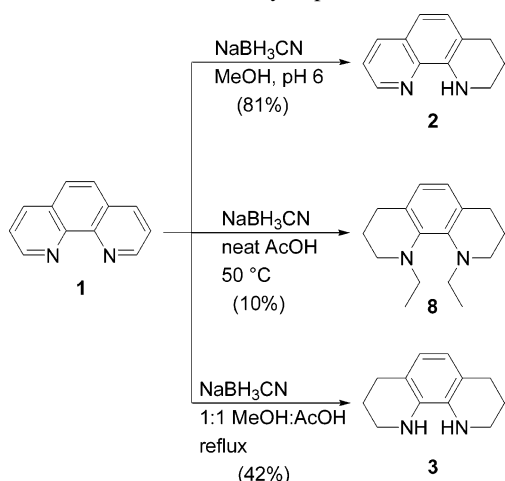
**Figure 2.** Examples of benzimidazole-based *N*-heterocyclic carbenes.

atoms (Figure 2). These substituents have typically been installed via aryl amination<sup>8</sup> or amidation chemistry<sup>11</sup> (6 and 7) or by direct *N*-alkylation<sup>7,9</sup> of benzimidazoles (5).

As part of a program aimed at ligand synthesis in our laboratory, we envisioned that 1,2,3,4,7,8,9,10-octahydro-1,10-phenanthroline (3, R = H), prepared by reduction of the pyridyl rings of 1,10-phenanthroline, could serve as a versatile precursor for a new class of benzimidazole-based NHCs (Figure 1). The successful preparation of such a compound would stimulate the development of chiral analogues with stereogenic centers  $\alpha$  to the nitrogen atoms of reduced 2-substituted and 2,9-disubstituted phenanthrolines (4).<sup>12</sup> It is anticipated that the greater rigidity afforded by the structural motif exemplified by 3 will lead to useful reagents for asymmetric transformations for subsequent chiral derivatives.

Our proposed *N*-heterocyclic carbene synthesis required a reasonable quantity (0.5–2 g) of 1,2,3,4,7,8,9,10-octahydro-1,10-phenanthroline 3 being prepared (Scheme 1).

**Scheme 1.** Alternate Preparation of 1,2,3,4,7,8,9,10-Octahydrophenanthroline



Although several methods are known for the preparation of 1,2,3,4-tetrahydro-1,10-phenanthroline (2) in moderate to good yields,<sup>3</sup> to the best of our knowledge, only two reports have appeared regarding the preparation of the octahydro

derivative (3). The first of these used borane reduction of 1,10-phenanthroline, giving a mixture of 2 and 3 in low (<10%) combined yield.<sup>13</sup> The second method employed high pressure and high-temperature hydrogenation of 1 with Raney nickel<sup>14</sup> [27.6 bar (400 psi), 100 °C for 36 h], providing 3 in 92% yield. We wished to explore a milder set of conditions with which to prepare 3. Previous reductions of 1,10-phenanthroline to the tetrahydro derivative (2) have used borohydrides such as Zn(BH<sub>4</sub>)<sub>2</sub> under sonication<sup>15</sup> or NaBH<sub>3</sub>CN/BF<sub>3</sub>·OEt<sub>2</sub> under anhydrous conditions,<sup>16</sup> which gave 2 in 80% and 70% yields, respectively. We thought it should be possible, with appropriate modification of these procedures, to elicit more complete reduction of 1–3.

Initial experiments (NaBH<sub>3</sub>CN, MeOH, pH 6) led only to isolation of 2 (Scheme 1). Addition of more NaBH<sub>3</sub>CN failed to advance the reduction to the desired octahydro product (3). Further reduction of 2 was likely hampered by the generation of the more basic piperidine-like nitrogen atom, and the acidity of the medium was insufficient to protonate the remaining aromatic nitrogen, a requirement in reductions of  $\pi$ -deficient pyridyl rings.<sup>17–19</sup> Performing the reaction in glacial acetic acid<sup>20</sup> as solvent would ensure the double protonation of nitrogens in tetrahydro intermediate 2, allowing the reduction to continue. Although this set of conditions did initially form octahydro 3, the product surprisingly reacted further, undergoing diethylation with concomitant decomposition to give the undesired *N*1,*N*10-diethyl-2,3,4,7,8,9-hexahydrophenanthroline (8) as the only isolable product in low 10% yield.<sup>21</sup> In an effort to disfavor the side reaction of 3 with acetic acid, we diluted the reaction mixture with methanol. Thus, subjection of 1,10-phenanthroline to NaBH<sub>3</sub>CN reduction in 1:1 MeOH and glacial acetic acid<sup>22</sup> at reflux provided the desired product 3 in a modest, but useable, 42% yield after purification.<sup>23</sup> This reduction process is operationally simple in that it can be

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(17) Review: Seller, R. V.; Reshetov, P. V.; Kriven'ko, A. P. *Chem. Heterocycl. Compds. (N.Y.)* **2001**, 37, 797.

(18) Hamilton, T. S.; Adams, R. *J. Am. Chem. Soc.* **1928**, 50, 2260.

(19) For reductions of *N*-alkylpyridinium salts, see: (a) Wenkert, E. *Acc. Chem. Res.* **1968**, 1, 78. (b) Liberatore, F.; Carelli, V.; Cardellini, M. *Tetrahedron Lett.* **1968**, 9, 4735. (c) Hutchins, R. O.; Natale, N. R. *Synthesis* **1979**, 281. (d) Lavilla, R.; Gotsens, T.; Gullón, F.; Bosch, J. *Tetrahedron* **1994**, 50, 5233. (e) McCullough, K. J.; MacTavish, J.; Proctor, G. R.; Redpath, J. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2553.

(20) Booker, E.; Eisner, U. *J. Chem. Soc., Perkin Trans. 1* **1975**, 929.

(21) For a similar reductive ethylation with NaBH<sub>4</sub> in AcOH, see: Gribble, G. W.; Lord, P. D.; Skotnicki, J.; Dietz, S. E.; Eaton, J. T.; Johnson, J. *J. Am. Chem. Soc.* **1974**, 96, 7812.

(22) The use of proportionately less acetic acid (e.g., 5:2 MeOH/AcOH) gave the undesired tetrahydro product 2.

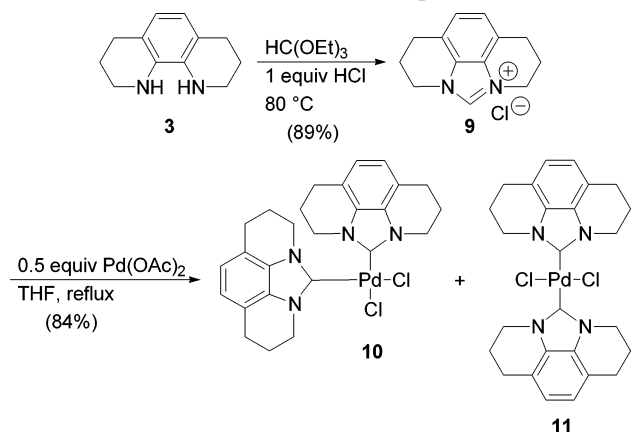
(23) With regards to the use of NaBH<sub>4</sub> or NaBH(OAc)<sub>3</sub> for the preparation of 3, results indicate that NaBH<sub>4</sub> is an inferior reducing agent to NaBH<sub>3</sub>CN in this reaction. The reaction stops at the stage of tetrahydro product 2, even under prolonged heating and with excess reagent. Since it is reasonable to assume that NaBH(OAc)<sub>3</sub> is produced in situ under the reaction conditions, this reagent can also be ruled out as an effective alternative to NaBH<sub>3</sub>CN for this process. Reactions performed in neat acetic acid were found to be difficult to control and stop at product 3. Oftentimes, 3 completely vanished from the reaction mixture (NMR monitoring) to give a large number of unidentifiable products, of which only 8 could be identified concretely after purification.

(12) For examples of oxazoline-derived imidazoliums, see: Glorius, F.; Altenhoff, G.; Goddard, R.; Lehmann, C. *Chem. Commun.* **2002**, 2704.

performed in air, requires no hydrogenation equipment, and can be scaled up without difficulty.

With diamine **3** in hand, we turned our attention to cyclization and NHC preparation. Treatment of **3** with neat triethyl orthoformate<sup>8</sup> containing 1 equiv of HCl provided the key tetracyclic benzimidazolium chloride **9** in 89% yield (Scheme 2). To test the propensity of **9** to act as a carbene

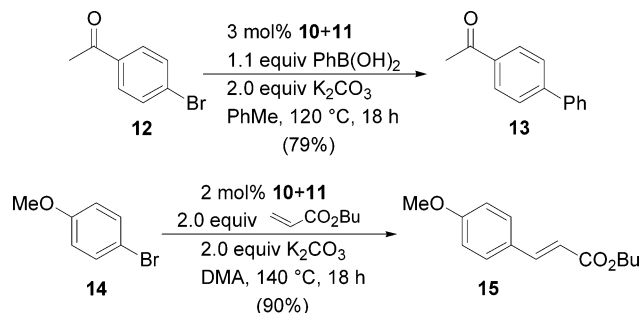
**Scheme 2.** Synthesis of Tetracyclic Benzimidazolium Chloride **9** and NHC Palladium Complexes **10** and **11**



ligand precursor, it was heated with 0.5 equiv of  $\text{Pd}(\text{OAc})_2$ <sup>11</sup> (THF, reflux, 1 h). The reaction mixture underwent a distinct color change from orange to light gray, from which a pale gray precipitate was collected. NMR and mass spectral analysis confirmed the formation of palladium complexes **10** and **11** as a 1:1 mixture of *cis* and *trans* coordination isomers,<sup>24</sup> isolated in 84% yield.<sup>25</sup>

Preliminary experiments have revealed that **10** + **11** is an active catalyst for C–C bond-forming reactions such as Suzuki–Miyaura and Heck couplings.<sup>26</sup> Subjection of 4-bromoacetophenone **12** to Suzuki–Miyaura coupling with phenylboronic acid in the presence of 3 mol % of **10** + **11** ( $\text{K}_2\text{CO}_3$ , PhMe, 120 °C, 18 h) gave biphenyl **13** in good 79% yield (Scheme 3). Alternatively, the more electron-rich 4-bromoanisole **14** reacts smoothly with butyl acrylate (2 mol % **10** + **11**,  $\text{K}_2\text{CO}_3$ , DMA, 140 °C, 18 h) to provide cinnamate **15** in excellent 90% isolated yield.

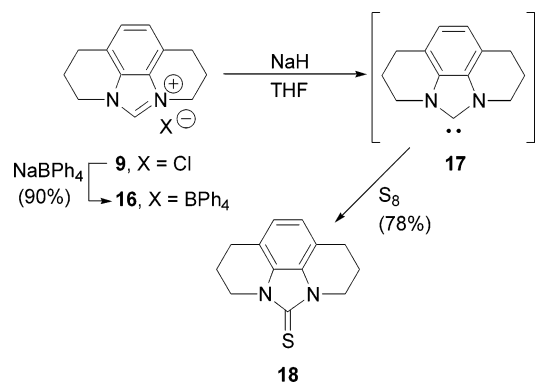
**Scheme 3.** Carbon–Carbon Bond-Forming Reactions Catalyzed by **10** + **11**



Previous benzimidazolium salts have been shown to serve as precursors to stable free carbenes via deprotonation when sufficiently bulky substituents are present on the nitrogens<sup>7,8</sup> (**5b**, **6**, Figure 2). Such NHCs are persistent under anhydrous conditions and typically display  $^{13}\text{C}$  NMR chemical shifts near  $\delta$  224–231<sup>7,8</sup> for the carbenoid carbon. In contrast, benzimidazolium salts with smaller *N*-methyl substituents (**5a**) have a propensity to dimerize<sup>7,27,28</sup> to the corresponding alkenes upon deprotonation. An exception to this is the *N*-methyl-*N*-ferrocenyl NHC **7** which, although it could not be characterized as the “free” carbene and did not show a tendency to dimerize, could be trapped with elemental sulfur to give the corresponding thiourea in a reaction typical of NHCs.<sup>11</sup>

To prepare a stable free carbene from **9**, the  $\text{Cl}^-$  counterion was exchanged for  $\text{BPh}_4^-$  (**16**) to improve solubility. Given the range of stabilities of previous benzimidazolium-derived NHCs, it was difficult to predict on the basis of steric or electronic factors which of the three preceding types of NHC (**5a**, **6**, or **7**) that compound **16** would behave like. Subsequent experiments revealed that the “free” NHC **17**, generated by treatment of **16** with KO-*t*-Bu or NaH in THF (Scheme 4), was too unstable to characterize by  $^1\text{H}$  and  $^{13}\text{C}$

**Scheme 4.** Trapping of NHC **17** with Sulfur To Give Thiourea **18**



NMR in  $\text{THF}-d_8$ . However, sequential deprotonation of **16** (NaH, THF, 1 h) followed by addition of elemental sulfur delivered the thiourea **18** in 78% yield. These results indicate that the tetracyclic NHC **17** closely resembles the behavior of *N*-ferrocenyl NHC **7**, both in the instability of its “free” carbene and in its lack of tendency to dimerize.

Current studies are underway to crystallographically characterize complexes **10** and **11**, as is the preparation of chiral

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(25) Compounds **10** and **11** are not separable by chromatography. *cis*-**10** is configurationally stable and does not isomerize to **11** even after prolonged heating (130 °C, 4 days) in  $\text{DMSO}-d_6$ , as determined by periodic  $^1\text{H}$  NMR monitoring. No change in the ratio of **10/11** was observed over this period.

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(27) Cetinkaya, E.; Hitchcock, P. B.; Kucukbay, H.; Lappert, M. F.; Al-Juaid, S. *J. Organomet. Chem.* **1994**, 481, 89.

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versions of **9**, including those derived from  $C_2$ -symmetric reduction products of 2,9-disubstituted phenanthrolines (**4**, e.g., neocuproine, R = Me). The greater rigidity of these NHCs afforded by the tetracyclic benzimidazole framework exemplified by **9** is anticipated to provide useful ligands and reagents for asymmetric synthesis. The results of these studies will be reported in due course.

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**Supporting Information Available:** Experimental procedures for **3**, **9–11**, **13**, **15**, **16**, and **18** and characterization data for all compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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