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A General Synthesis of End-Functionalized Oligoanilines via Palladium-Catalyzed Amination

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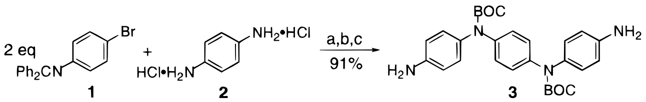
Polyaniline has attracted much attention in the field of organic conducting polymers due to its robust nature in the doped emeraldine state.[1] Among the many industrial applications it has found are its use as components in rechargeable batteries,[2] electromagnetic interference shielding,[3] and anticorrosion coatings for steel.[4]

In 1986, Wudl and co-workers demonstrated that synthetically prepared phenyl-capped octaaniline exhibited properties similar to bulk polyaniline (comparable UV/vis, IR, CV, and conductivity).[5] Consequently, an octaaniline could be considered a good model or substitute for applications involving polyaniline. Aside from the modified Honzl condensation method Wudl employed for synthesizing oligoanilines, other methods of preparation include titanium-alkoxide-mediated couplings with aniline derivatives,[6] Ullmann couplings,[7] and an adaptation of the Willstätter−Moore approach.[8] All of these methods have yet to demonstrate generality in the choice of substrates for carrying out oligomerizations and have the common drawback of lacking the ability to functionalize end groups.

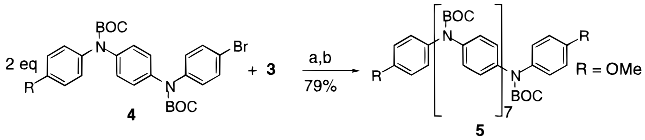
We desired to expand the repertoire of techniques available for constructing oligoanilines and their analogues to include a strategy based on Pd-catalyzed amination methodology. We speculated that such a method would demonstrate efficiency in the preparation of oligoanilines and derivatives due to the broad scope of the Pd-catalyzed amination reaction.[9] To undertake such an objective, three issues had to be confronted. First, an orthogonal protecting group strategy had to be developed to differentiate internal and terminal nitrogens. Second, a means of masking or selectively introducing terminal bromides for use in couplings with aniline derivatives had to be implemented. Third, and most importantly, construction would have to be carried out in a bidirectional mode to produce materials with symmetry. Herein, we report our first efforts toward a unified strategy for synthesizing oligoanilines with end group functionalization. In light of Wudl's pioneering studies,[5] we initially chose to target functionalized octaanilines.

Scheme 1[a]



[a] Reagents and conditions: (a) $Pd(OAc)_2$ (1 mol %), BINAP (1.5 mol %), NaO^tBu (4.5 equiv), toluene, 80 °C; (b) $(BOC)_2O$ (3 equiv), 4-DMAP (0.1 equiv), THF/toluene, reflux; (c) (i) $HONH_2{\cdot}HCl$ (2.5 equiv), pyridine, $CHCl_3$/THF/EtOH, rt, (ii) Et_3N.

Scheme 2[a]



[a] Reagents and conditions: (a) $Pd_2(dba)_3$ (2 mol %), BINAP (5 mol %), NaO^tBu (2.5 equiv), toluene, 80 °C; (b) $(BOC)_2O$ (3 equiv), 4-DMAP (0.1 equiv), THF, reflux.

As a surrogate for 4-bromoaniline in the controlled construction of oligoanilines we used *N*-(diphenylmethylene)-4-bromoaniline (**1**) (Scheme 1).[10] The imine group serves the dual purposes of protecting the nitrogen and activating the compound to oxidative addition to the Pd catalyst. To build symmetrical oligomers we employed 1,4-phenylenediamine dihydrochloride (**2**) as a core piece for initiating two-directional growth. We found that coupling took place smoothly using **1** (2 equiv) and **2** (1 equiv) in the presence of $Pd(OAc)_2$ (1 mol %), BINAP (1.5 mol %), and NaO^tBu (4.5 equiv) in toluene at 80 °C. To avoid oxidation of the desired product, each of the internal amines was protected, in situ, as a *tert*-butyl carbamate (BOC) by addition of $(BOC)_2O$ and a catalytic amount of 4-(dimethylamino)pyridine (DMAP). The crude diphenyl ketimine product was cleaved with hydroxylamine hydrochloride[11] to afford **3** in an overall yield of 91%.

Two approaches were taken to complete the assembly of the octamers. The first strategy (Scheme 2) entails coupling diamine **3** with bromide **4** (2 equiv)[12] followed by BOC-protection of the initially formed intermediate. The 4-methoxyphenyl-capped octamer (**5**, R = OMe) was constructed in this manner in 79% yield.

While this first strategy (Scheme 2) is highly convergent, a second route was adopted for the purpose of rapidly building a family of octaanilines from a common precursor as shown below in Scheme 3. This alternative route commences with a Pd-catalyzed coupling of **3** and **8** (see below) to produce **9** after in situ BOC-protection (74%). Diamine **10** was obtained in 86% by hydrogenolysis of **9** with $Pd(OH)_2$/carbon and ammonium formate. Capping **10** by Pd-catalyzed coupling with the appropriate aryl bromide (followed by in situ BOC-protection) provided the desired octaaniline (77−82%). Octamers (**5**) capped with R = H, *tert*-butyl, dodecyl, and cyano were prepared in this fashion and were found to be soluble in most common organic solvents.[13]

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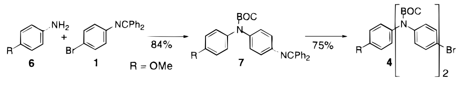
[12] Precursor **4** was prepared in two isolated steps. Intermediate **7** was isolated in 84% yield following a Pd coupling and in situ BOC-protection. Hydrogenolysis of **7**, followed by coupling with 1,4-dibromobenzene and in situ BOC-protection afforded **4** in 75% yield. For experimental details, see the Supporting Information.



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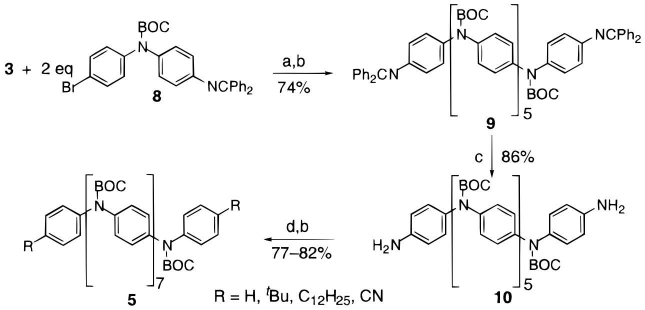
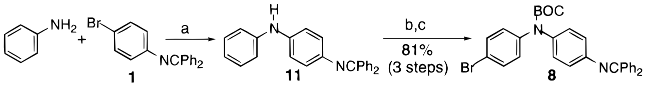
Scheme 3[a]



[a] Reagents and conditions: (a) $Pd(OAc)_2$ (6 mol %), BINAP (7 mol %), NaO^tBu (2.8 equiv), toluene, Et_3N, 90 °C; (b) $(BOC)_2O$ (3 equiv), 4-DMAP (0.1 equiv), THF, reflux; (c) 20% $Pd(OH)_2/C$ (0.4 equiv), $(NH_4)HCO_2$ (20 equiv), THF/EtOH (2:1), 70 °C; (d) RC_6H_4Br (2.1 equiv), $Pd_2(dba)_3$ (2 mol %), BINAP (6 mol %), NaO^tBu (2.5 equiv), THF, reflux.

Scheme 4[a]

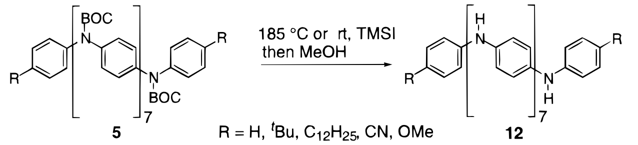


[a] Reagents and conditions: (a) $Pd_2(dba)_3$ (0.1 mol %), BINAP (0.24 mol %), NaO^tBu (1.4 equiv), THF, reflux; (b) Bu_4NBr_3, CH_2Cl_2, rt; (c) $(BOC)_2O$ (1.5 equiv), 4-DMAP (0.05 equiv), THF, reflux.

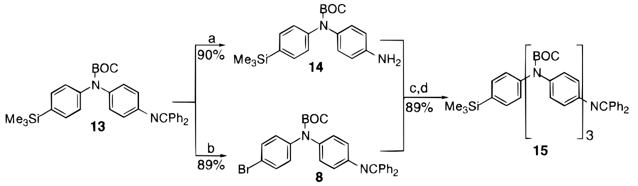
Essential to the efficiency of this route is the facile construction of **8** as illustrated in Scheme 4. Coupling of **1** with aniline with $Pd_2(dba)_3$ (0.1 mol %) (dba = dibenzylideneacetone) and BINAP (0.24 mol %) proceeded cleanly to give intermediate **11**. Regioselective bromination followed by BOC-protection of the crude coupling product (**11**) provided **8** in 81% yield for the 3-step sequence.[14]

The BOC groups throughout the backbone of the octamers prevent oxidation of the material and ease its handling by improving solubility.[15] The BOC groups were removed quantitatively either by thermolysis[16] (185 °C, 9 h), or by treatment with TMSI[17] at room temperature in CH_2Cl_2, followed by addition of triethylamine and methanol. Analysis by ^1H NMR, IR, and UV/vis spectroscopies indicated that the deprotection was clean in each case producing octaanilines in the leucoemeraldine state. When these materials were oxidized to the emeraldine state[18] under acidic conditions, we observed, by UV/visible spectroscopy, an absorption between 700 and 1000 nm, characteristic of the narrow bandgap in oligoanilines and polyaniline.[5b]

Scheme 5



Scheme 6[a]



[a] Reagents and conditions: (a) $(NH_4)HCO_2$ (12 equiv), 10% Pd/C (0.1 equiv), EtOH, 60 °C; (b) Br_2, NaOAc, THF, 0 °C; (c) $Pd_2(dba)_3$ (2 mol %), BINAP (5 mol %), toluene, 80 °C; (d) $(BOC)_2O$ (1.5 equiv), 4-DMAP (0.1 equiv), THF, reflux.

Oligoanilines other than octamers or tetramers (capping of **3**) are accessible by appending different side chains to **3**. Toward this end, we developed a divergent/convergent approach[19] (Scheme 6) to build nonsymmetrical oligomers. The key component in this strategy is **13**, prepared from the Pd-catalyzed coupling of 4-(trimethylsilyl)aniline[20] with **1**, followed by in situ BOC protection. One portion of **13** was subjected to hydrogenolysis, affording amine **14**, and a second portion was regioselectively brominated to produce **8**. The combination of **14** and **8** was subjected to Pd-catalyzed amination. After in situ BOC protection of the crude product, **15** was obtained in 89% yield. This process may be used to construct oligomers of longer chain lengths, doubling in length with each iteration.

This new approach to constructing oligoanilines should prove to be general in nature for building oligomers of any length by combining the products assembled from the divergent/convergent strategy with various symmetrical building blocks (**2**, **3**, **10**, or others[21]). The current work provides octaanilines with flexibility in modification of the end groups. In addition, protecting the amines as *tert*-butyl carbamates facilitates manipulations of the materials by impeding oxidation and solubilizing the oligoaniline. The syntheses of the materials can be efficiently carried out on a multigram scale since all intermediates and end products were isolated as solids by recrystallization or precipitation.[22] Electrochemical studies as well as the preparation of oligoanilines of varying chain length are in progress and will be reported in due course.

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Supporting Information Available: Experimental details and characterization data (13 pages). See any current masthead page for ordering and Internet access instructions.

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(13) The BOC-protected oligomers (**5**) were quite soluble in solvents such as CH_2Cl_2, EtOAc, THF, and Et_2O; however, the deprotected oligoanilines were only sparingly soluble in polar solvents such as DMF or NMP, as observed in previous studies.[5−8]

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(15) An additional benefit of the BOC group lies in its ability to activate toward Pd oxidative addition substrates which contain a secondary aromatic amine para to a bromide (such as **4** or **8**). In the absence of BOC-protection, such substrates generally fail to couple with amines under standard Pd-catalyzed amination conditions.

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(21) Odd-numbered oligoanilines should be accessible from $(p\text{-}H_2NC_6H_4)_2N$-BOC (in place of **3** in Scheme 2) which may be derived from 4,4′-dibromodiphenylamine as described in: Wolfe, J. P.; Åhman, J.; Sadighi, J. P.; Singer, R. A.; Buchwald, S. L. *Tetrahedron Lett.* **1997**, *38*, 6367−6370.

(22) All isolated intermediates and products (**3**−**5**, **7**−**10**, **13**−**15**) were characterized by ^1H and ^{13}C NMR spectroscopy, IR, and elemental analysis.