Directly Fused Highly Substituted Naphthalenes via Pd-Catalyzed Dehydrogenative Annulation of N,N-Dimethylaminomethyl Ferrocene Using a Redox Process with a Substrate

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ABSTRACT

N,N-Dimethylaminomethyl ferrocenium could be generated in situ and served as a terminal oxidant for Pd-catalyzed directly dehydrogenative annulations of N,N-dimethylaminomethyl ferrocene and internal alkynes. This procedure utilized the redox activity of ferrocene and avoided adding an oxidant. A series of highly arylated naphthalenes functionalized by ferrocene were obtained in 53–81% yields.

Polycyclic aromatic hydrocarbons with condensed aromatic cores have attracted considerable attention because of their electrochemical and photochemical properties and their applications in π-conjugated functional materials, such as organic semiconductors and luminescent materials. Arguably, highly arylated naphthalenes represent one of the most important classes of polycyclic aromatic compounds because the aryl group could enhance their fluorescent properties in the solid state and their ability to transport charge. Numerous synthetic methodologies for building such a structure have been developed in the past decades, among which metal-catalyzed activation of C–H bonds in arenes followed by coupling with alkynes has been recognized as an increasingly important tool. Recently, Miura, Wu and our group have obtained polyaryl naphthalenes via the metal (Pd, Rh) catalyzed dual C–H bonds activation of benzene derivatives (Scheme 1). These procedures

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occur with a high valent metal as an initiator (such as Pd\(^{11}\) for a Pd-catalyst) and generate a lower valent metal, such as Pd\(^0\). Therefore, the stoichiometric oxidant, such as Cu(OAc)\(_2\), AgOAc, and K\(_2\)S\(_2\)O\(_8\), was required to complete the catalytic cycle.

On the other hand, the cyclopentadienyl (Cp) of ferrocene is easily modified. The electro- and photochemical properties of the Fe(II)Cp\(_2\) fragment can be tuned by selecting the substituent introduced to the Cp ring.\(^6\) Therefore, the electro- and photochemical properties of naphthalenes could be regulated by modifying the ferrocene ring. In 1989, Micheal Pfeffer and co-workers reported a synthetic protocol to generate ferrocene-containing naphthalenes from \(N, N\)-dimethylaminoferrocenyl ferrocene with alkynes by annihilation reactions.\(^7\) In this process, a stoichiometric amount of palladium was required (Path A, Scheme 2).

The challenge existed for ferrocene derivatives as a substrate to construct such a structure through metal-catalyzed dual \(C-H\) activation since the ferrocene unit suffered from being oxidized into ferrocenium by an external oxidant. Ferrocenium was a prototypically outer-sphere one-electron oxidant routinely used in some reactions.\(^8\) It was deduced that ferrocene with a directing group could serve as a substrate for the transition-metal-catalyzed dual \(C-H\) activation without adding oxidant due to its redox property. In our continuing effort to develop a versatile dehydrogenative coupling reaction under external oxidant-free conditions,\(^9\) we explored the Pd-catalyzed (10 mol % catalyst loading) synthesis of ferrocene functionalized naphthalenes from \(N, N\)-dimethylaminoferrocenyl ferrocene with alkynes in one step under air (Path B, Scheme 2). The \(N, N\)-dimethylaminoferrocenyl ferrocene could be generated by air \textit{in situ} and serve as a terminal oxidant in this process.

To test our hypothesis, first we examined the reaction of \(N, N\)-dimethylaminomethyl ferrocene 1 with diphenylacetylene 2a in the presence of 10 mol % Pd(OAc)\(_2\), K\(_2\)PO\(_4\) as a base, and TBAB as the additive in DMA at 90 °C. The main product was obtained in 53% yield (Table 1, entry 1), which was characterized and proven to be the desired product 3a by NMR and MS. Inspired by this result, we optimized the reaction conditions by using 10 mol % Pd(OAc)\(_2\) as the catalyst. Except for K\(_3\)PO\(_4\), other bases, such as K\(_2\)CO\(_3\), KHCO\(_3\), and Na\(_2\)CO\(_3\) (Table 1, entries 2–4), were screened. K\(_2\)CO\(_3\) proved to be the most effective for this transformation and gave a 64% yield (Table 1, entry 2).

The yield increased to 81% from 64% when the reaction temperature increased to 110 °C from 90 °C (Table 1, entry 5). Only a 10% yield was obtained when the reaction was carried out under a N\(_2\) atmosphere (Table 1, entry 6). When the loading of Pd(OAc)\(_2\) was reduced from 10 mol % to 5 mol % and 1 mol %, the yield decreased to 72% and 37%, respectively (Table 1, entries 8 and 9). The optimal reaction conditions were determined: Pd(OAc)\(_2\) (10 mol %), K\(_2\)CO\(_3\) (1.0 equiv), TBAB (0.25 equiv), DMA, 110 °C, 48 h, under air.

Under the optimal reaction conditions, the scope of the substrates was investigated (Figure 1). The results showed

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\(\text{Scheme 1. Transition-Metal-Catalyzed Cycloaddition of Arenes with Disubstituted Alkynes}\)

\(\text{Scheme 2. Pd-Catalyzed Annulation Reaction of } N,N\text{-Dimethylaminoferrocene with Diphenylacetylene}\)

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that N,N-dimethylaminomethyl ferrocene 1 reacted smoothly with diphenylacetylene and its derivatives 2a–2d, providing the corresponding products in 57–81% yields (3a–3d, Figure 1). p-Fluoro-substituted diphenylacetylene afforded product 3e in only 35% yield under the optimized reaction conditions. It was noted that the yield could increase to 61% by lowering the temperature down to 100 °C. A similar result happened for p-trifluoromethyl-substituted diphenylacetylene. The yield dramatically increased to 76% from 37% in the absence of K2CO3 and TBAB at 70 °C (for 3f, Figure 1), while the optimized catalytic system was applied to unsymmetrical diarylacetylene. Trimethyl[4-(phenyl-ethynyl)phenyl]silane and 1-methyl-4-(phenyl-ethynyl)benzene gave the corresponding desired products in 61% and 53% yields, respectively. Nevertheless, the regioselectivity was poor.

To clarify the reaction mechanism, controlled experiments were designed (Scheme 3). When N,N-dimethylaminomethyl ferrocene was treated with diphenylacetylene in the presence of Pd(OAc)2 (10 mol %), TBAB (0.25 equiv) in NMP at 90 °C for 48 h without K2CO3, the desired product 3a and the intermediate C were obtained in 5% and 8% yields, respectively (eq 1, Scheme 3). Meanwhile, a 34% yield of 3a was achieved in the presence of K2CO3 (eq 2, Scheme 3). These results indicated that the base, such as K2CO3, played a key role in the cycloaromatization step.

Moreover, subproduct 4 with a red color was obtained under the reaction conditions shown in eq 1, Scheme 3. Compound 4 was isolated easily from the reaction mixture by chromatography on silica gel, since it exhibited a much lower Rf value than the starting materials and the desired product. Fortunately, its single crystal was developed successfully and characterized by X-ray diffraction. An ORTEP drawing is shown in Figure 2. The palladium atom was coordinated with two double C–C bonds and a N-atom.

Based on the results above, the reaction mechanism for the cycloaromatization of 1 with diphenylacetylene 2a was proposed and illustrated in Scheme 4. First, cyclopalladated...
**Scheme 4.** Plausible Reaction Mechanism for the Cyclization Reaction

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Figure 2. Molecular structure of 4.

\(N,N\)-dimethylaminomethyl ferrocene A was formed via coordination of the palladium atom to the N-atom and subsequently electrophilic attack at the 2-position carbon atom. Then, the palladacycle A was coordinated with alkyne 2a, followed by syn-insertion to give intermediate B. Subsequent cis-trans isomerization in B and B' may take place,\(^{(2c,7a,10)}\) and the second alkyne was inserted to give the intermediate C. The subproduct 4 may come from intermediate C since the methyl group is easily replaced by a H-atom. Intermediate C' was formed from intermediate C.\(^{(11)}\) Next, the intramolecular 5-exo-dig insertion\(^{(11a,12)}\) of a benzene led to spiro palladium intermediate D. The subsequent bond migration and reductive elimination generated the cyclic product as well as Pd\(^{0}\) species that can be reoxidized into the active Pd\(^{II}\) species by \(N,N\)-dimethylaminomethyl ferrocenium to complete the catalytic cycle. \(N,N\)-Dimethylaminomethyl ferrocene was easily oxidized into \(N,N\)-dimethylaminomethyl ferrocenium and serve as an oxidant. To examine this hypothesis, the transformation was monitored by a high resolution ESI-FTMS technique. The species of \(N,N\)-dimethylaminomethyl ferrocenium was observed (principal ion of \(m/z\) 243.0700; calcd for \(C_{13}H_{17}FeN^{+}\): \(m/z\) 243.0710; Figure S1).

In summary, we have developed a novel protocol to successfully build ferrocene functionalized naphthalenes via Pd-catalyzed direct dehydrogenative annihilations of \(N,N\)-dimethylaminomethyl ferrocene and internal alkyne. \(N,N\)-Dimethylaminomethyl ferrocenium was generated in situ and served as a terminal oxidant. This procedure utilized the redox activity of ferrocene and avoided adding an oxidant, which made this approach “greener” and easier to handle. Further investigations on the detailed reaction mechanism and fluorescent properties of products are ongoing.

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**Supporting Information Available.** Experimental details and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

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