ORGANIC LETTERS

2012
Vol. 14, No. 12
3012–3015

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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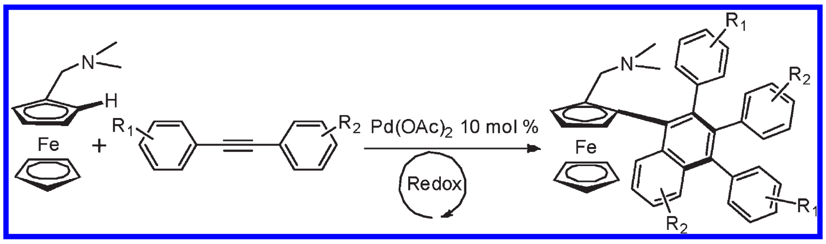
Received April 23, 2012

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.[1] Arguably, highly arylated naphthalenes represent one of the most important classes of polycyclic aromatic compounds because the aryl group could enhance their fluoresent properties in the solid state and their ability to transport charge.[2] Numerous synthetic methodologies for building such a structure have been developed in the past decades,[3] among which metal-catalyzed activation of C–H bonds in arenes followed by coupling with alkynes has been recognized as an increasingly important tool.[4] 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).[2a–c,3c,5] These procedures

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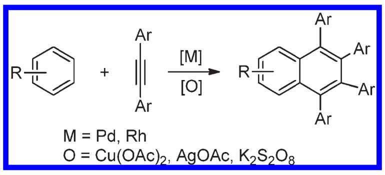
10.1021/ol301063k
Published on Web 05/24/2012

occur with a high valent metal as an initiator (such as Pd^{II} 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 $K_2S_2O_8$, was required to complete the catalytic cycle.

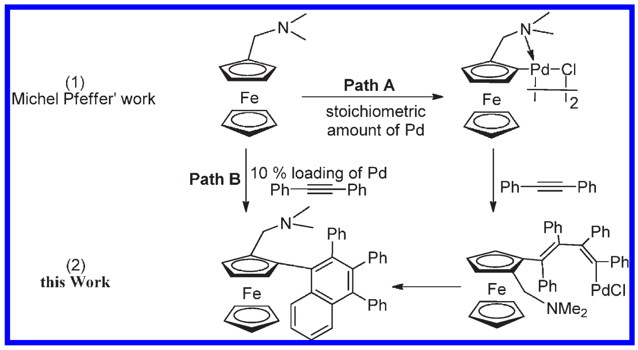
Scheme 1. Transition-Metal-Catalyzed Cycloaddition of Arenes with Disubstituted Alkynes



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*-dimethylaminomethyl ferrocene with alkynes by annulation 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*-dimethylaminomethyl ferrocene with alkynes in one step under air (Path B, Scheme 2). The *N*,*N*-dimethylaminomethyl ferrocenium could be generated by air *in situ* and serve as a terminal oxidant in this process.

Scheme 2. Pd-Catalyzed Annulation Reaction of *N*,*N*-Dimethylaminomethylferrocene with Diphenylacetylene



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_3PO_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_3PO_4, other bases, such as K_2CO_3, $KHCO_3$, and Na_2CO_3 (Table 1, entries 2−4), were screened. K_2CO_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_2CO_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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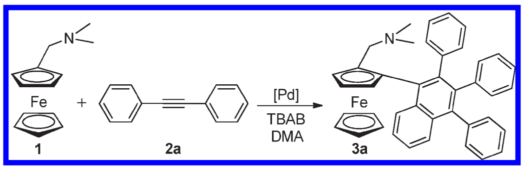
Table 1. Pd-Catalyzed Cyclization of **1** with Alkyne **2a**[a]



entry	$Pd(OAc)_2$ (eqiuv)	base	temp (°C)	time (h)	yield (%)[b]
1	0.1	K_3PO_4	90	48	53
2	0.1	K_2CO_3	90	48	64
3	0.1	$KHCO_3$	90	48	43
4	0.1	Na_2CO_3	90	48	47
5	0.1	K_2CO_3	110	48	81
6	0.1	K_2CO_3	110	48	10[c]
7	0.1	K_2CO_3	110	24	60
8	0.05	K_2CO_3	110	48	72
9	0.01	K_2CO_3	110	48	37

[a] Reaction conditions: **1** (0.5 mmol), **2a** (1.15 mmol), $Pd(OAc)_2$ (10 mol %), base (0.5 mmol), additives (0.125 mmol), solvent (1.5 mL). [b] Isolated yield. [c] Under N_2.

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 K_2CO_3 and TBAB at 70 °C for 12 h (**3f**, Figure 1), while the optimized catalytic system was applied to unsymmetrical diarylacetylene. Trimethyl[4-(phenylethynyl)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 K_2CO_3, 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 K_2CO_3 (eq 2, Scheme 3). These results indicated that the base, such as K_2CO_3, 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 chromatograpy on silica gel, since it exhibited a much lower R_f 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

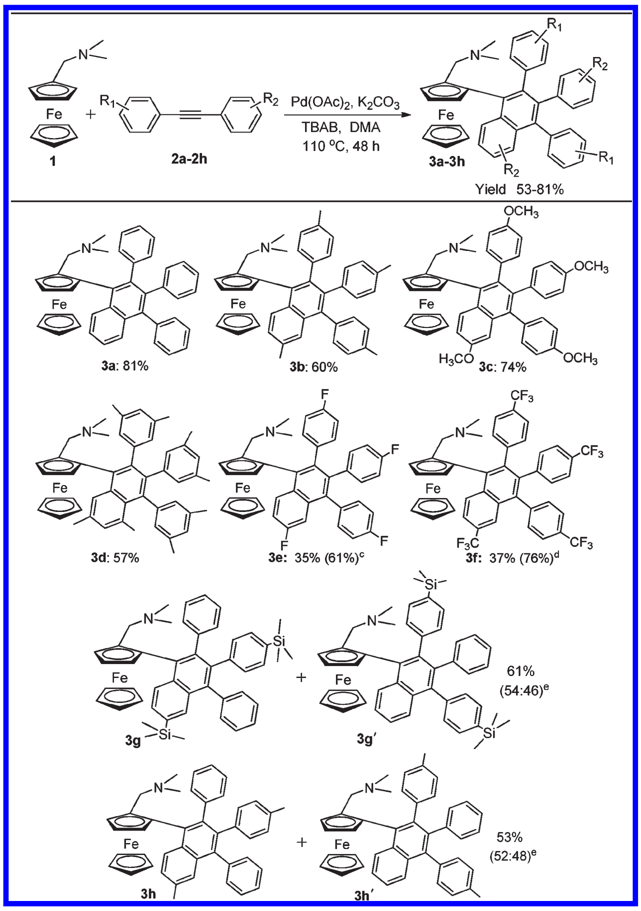
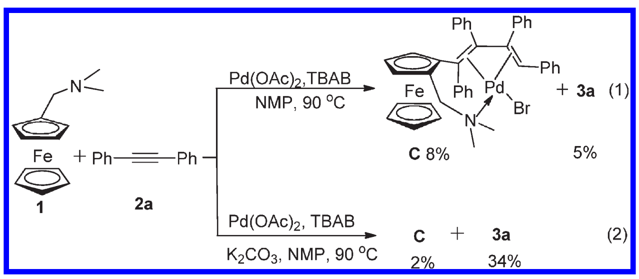


Figure 1. Pd-catalyzed cyclization of **1** with alkynes. Standard reaction conditions: **1** (0.5 mmol), **2** (1.15 mmol), $Pd(OAc)_2$ (10 mol %), K_2CO_3 (0.5 mmol), TBAB (0.125 mmol), DMA (1.5 mL), 110 °C 48 h. TBAB = tetrabutylammonium bromide. DMA = dimethyl acetamide. Isolated yields are provided. For **3e**, the temperature was 100 °C. For **3f**, the reaction was carried out without K_2CO_3 and TBAB at 12 h and 70 °C. For **3g** and **3h**, the ratio of the isomers in the parentheses were determined by ^1H NMR spectra analyses.

Scheme 3. Controlled Experiments



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

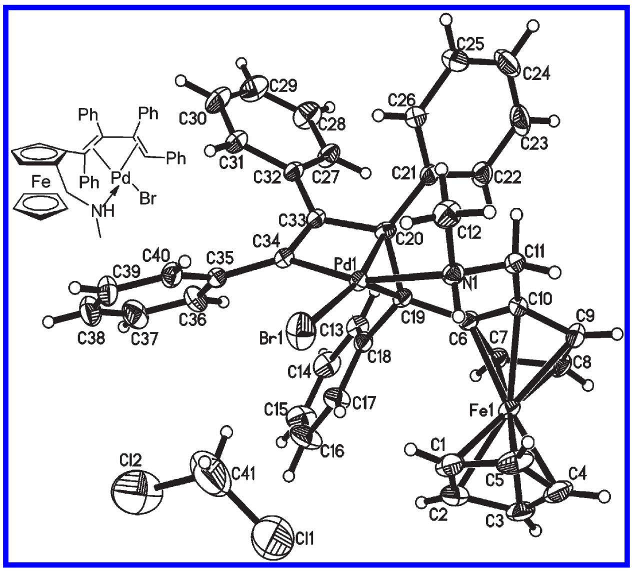
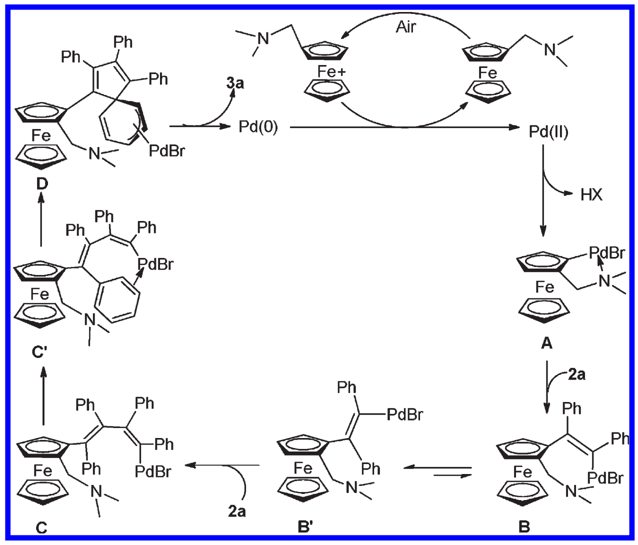


Figure 2. Molecular structure of **4**.

Scheme 4. Plausible Reaction Mechanism for the Cyclization Reaction



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 annulations of *N*,*N*-dimethylaminomethyl ferrocene and internal alkynes. *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.

Acknowledgment. We are grateful to the NSF of China (20972139, 21102133, 21172200) and the NSF of Henan (082300423201).

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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