



Catalytic C–H arylation of unactivated heteroaromatics with aryl halides by cobalt porphyrin

Ying Ying Qian, Ka Lai Wong, Meng Wen Zhang, Tsz Yiu Kwok, Ching Tat To, Kin Shing Chan*

Department of Chemistry, The Chinese University of Hong Kong, Shatin, New Territories, Hong Kong, People's Republic of China

ARTICLE INFO

Article history:

Received 18 November 2011

Revised 30 December 2011

Accepted 13 January 2012

Available online 21 January 2012

Keywords:

C–H arylation

Cobalt porphyrin

Heteroaromatics

Heterobiaryl

ABSTRACT

Direct C–H arylation of unactivated heteroaromatics with aryl halides catalyzed by cobalt porphyrin is reported. The reaction is proposed to go through a homolytic aromatic substitution reaction. The aryl radical is electrophilic and a SOMO–HOMO interaction is predominant in the aryl radical addition process.

© 2012 Elsevier Ltd. All rights reserved.

Heterobiaryls are very important structural motifs as they are commonly found in drugs, natural products, and optoelectronic materials.¹ 2-Acylhydrazino-5-arylpyrrole derivatives are used as antifungal reagents against *Candidae* (Fig. 1a).² The potential HIV-integrase inhibitor is constituted of an arylfuran moiety (Fig. 1b).³ 2-Arylpyrrole is the precursor of a potential anti-inflammatory and analgesic agent 5-aryl-1,2-dihydro-1-pyrrolizones.⁴ Therefore, facile and convenient syntheses of heterobiaryls are attractive.

Transition metal catalysts have been widely used in cross-coupling reactions to construct heterobiaryls.^{5–10} Heterobiaryls were first synthesized from heteroarylsilanes and aryl halides with a stoichiometric use of copper(I) salt.⁵ 2- and 3-arylfurans have been prepared by the nickel-catalyzed cross-coupling of 2- and 3-halofurans with aryl Grignard reagents.⁶ Later, heterobiaryls synthesized by the palladium-catalyzed Kumada,⁷ Suzuki–Miyaura,⁸ Stille^{9,1d} and Hiyama¹⁰ cross-couplings have also been reported. However, palladium catalysts and preactivation of heteroaromatics are required in most of the works.

Utilization of cheap and more abundant transition metal complex as a catalyst for the direct C–H arylation is attractive. Recently, 1st row transition metal catalysts have gained much attention in cross-coupling reactions. They are much cheaper and less toxic, such as Fe and Ni.^{1a,c,5} On the other hand, the direct C–H arylation of heteroaromatics with aryl halides have been achieved in some heterocycles, such as oxazoles, 1,2,3-triazoles, and indoles.¹¹ Direct C–H arylation avoids preactivation of heteroaromatics, which is

user-friendly and cost-effective. However, cobalt remains less-explored as a catalyst for the direct C–H arylation of heteroaromatics. Recently, we have reported the cobalt(II) porphyrin-catalyzed direct C–H arylation of unactivated arenes with aryl halides.¹² The reaction mechanism was proposed to proceed through a homolytic aromatic substitution followed by hydrogen atom abstraction to give the corresponding biaryls. However, the electronic influence on the homolytic aromatic substitution process remains unclear. This led us to turn our attention to both electron rich and poor heteroaromatics, for investigation of the electronic effect of aryl radical addition onto the heteroaromatics and the synthesis utility. Herein, we report the successful direct C–H arylation of heteroaromatics with aryl halides to give the heterobiaryls. Electron rich heteroaromatics reacted faster suggesting the importance of the electrophilic aryl radical in homolytic aromatic substitution.

Both π -excessive pyrrole and furan underwent successful direct C–H arylation with aryl halides (Table 1). In the presence of a catalytic amount of Co^{II}(tap) (tap = tetrakis-4-anisylporphyrinato dianion) (5 mol %), together with KOH (10 equiv) and ^tBuOH (10 equiv), 4-iodotoluene (1 equiv) was successfully coupled with pyrrole

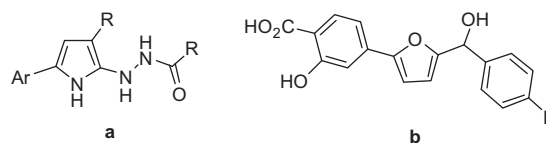
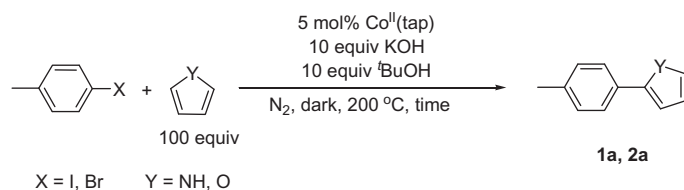


Figure 1. (a) Structure of 2-acylhydrazino-5-arylpyrrole derivatives; (b) structure of HIV-integrase inhibitor candidate.

* Corresponding author. Tel.: +852 39436376; fax: +852 26035057.

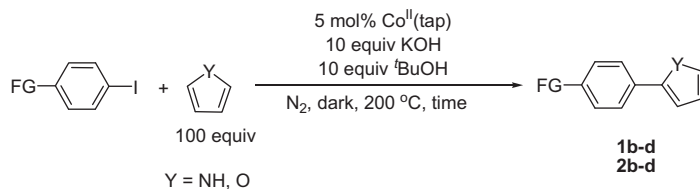
E-mail address: ksc@cuhk.edu.hk (K.S. Chan).

Table 1
Cobalt-catalyzed arylation of pyrrole and furan with 4-halotoluenes



Entry	Aryl halide	Solvent	Time (min)	Product	Yield (%)
1			15		74
2			30		52
3			60		62
4			60		42

Table 2
Cobalt-catalyzed arylation of pyrrole and furan with aryl iodides



Entry	Aryl halide	Solvent	Time (min)	Product	Yield (%)
1			30		54
2			30		69
3			30		66
4			60		49
5			60		52
6			60		62

(100 equiv) at 200 °C under N₂ to give a 74% yield of 2-(4-methylphenyl)pyrrole **1a** in only 15 min (Table 1, entry 1). When furan was used instead of pyrrole, a longer reaction time of 1 h was required for completion (Table 1, entry 3).

Arylbromides reacted slower than aryl iodides (Table 1). 4-Bromotoluene reacted with pyrrole and furan to give the corresponding coupling products **1a** and **2a** in 52% and 42% yields, respectively. However, the reaction took longer time and gave lower yields of the products. The weaker carbon–iodine bond (65.0 kcal/mol)¹³ of 4-iodotoluene compared with the carbon–bromine bond (80.4 kcal/mol)¹³ in 4-bromotoluene accounts for the

higher reactivity. The Ar–halogen bond cleavage is likely the rate-limiting step.

The direct C–H arylation is general for both electron rich and electron deficient aryl iodides. Pyrrole and furan reacted with electronically different 4-chloriodobenzene, iodobenzene, and 4-iodoanisole to give the corresponding coupling products in good yields in similar time (Table 2, entries 1–6). Therefore, the electronic effect of aryl radicals is not significant in this reaction system. This agrees well with the orthogonal nature of the sp² radical orbital to the delocalized π system in an aryl radical rendering the inductive effect through σ-bond insignificant.

Download English Version:

<https://daneshyari.com/en/article/5265495>

Download Persian Version:

<https://daneshyari.com/article/5265495>

[Daneshyari.com](https://daneshyari.com)