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Catalytic activity of chelating *N*-heterocyclic carbene palladium complexes towards selective phosphorylation of coumarins

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ABSTRACT

The catalytic activity of a series of heteroaryl coordinated chelating *N*-heterocyclic carbene (NHC) palladium complexes bearing different N-substituents, NHC backbones and chelating rings towards the phosphorylation of coumarins, and the relationship between the activity and the structure are presented. The results showed that the chelating NHC palladium complex **Ia–b** bearing the most σ-donating backbone and a more rigid five-membered chelating ring showed the highest efficiency. Using $AgNO_3$ as oxidant, a wide range of coumarins reacted with different dialkyl phosphite or diphenylphosphine oxide smoothly in CH_3CN, producing the target product in moderate to high yields.

1. Introduction

N-Heterocyclic carbenes (NHCs) have evolved into one of the most powerful tools in organic chemistry since the successful isolation and characterization of the first stable one by Arduengo and co-workers in 1991 [1]. Duo to their inherent characteristics of strong σ-donor and comparatively weak π-acceptor abilities, and facilely modifiable steric and electronic properties, NHCs have rivalled the traditionally widely used phosphine ligands in the fields of organic chemistry [2]. NHC complexes have been reported for all transition metals [3] and by far the largest application of NHC transition metal complexes is in various catalytic organic transformations, even with numerous successful application in commercially important processes. However, the most extensively studied NHC metal catalysed reactions are Ir- and Rh-catalysed hydrogenation and hydrogen transfer reaction [4], Rh- and Pt-catalysed hydrosilylation [5], Au-catalysed activation of π-bond [6], Ru-catalysed olefin metathesis [7], and Pd-, Ni-, or Fe-catalysed cross-coupling reactions [8]. Since the first NHC palladium catalysed Mizoroki-Heck reaction reported by Herrmann and co-workers [9], multiple kinds of NHC palladium complexes have been prepared and employed as highly active and robust catalysts for different carbon-carbon, or carbon-heteroatom cross-coupling reactions. It has been well documented that the electronic and steric characters of NHCs show enhancement at various steps of the catalytic circle, and then lead to improved catalytic activity [2a]. As NHCs bearing additional coordinating atoms form active species possessing increased stability and activity resulted from the chelating effects, the chelating/pincer NHC metal complexes have been studied extensively in catalysis [10]. The chelating/pincer palladium complexes have been proved to be highly efficient catalyst for the Heck reaction of vinyl compounds with aryl bromides and chlorides, Suzuki-Miyaura cross-coupling of aryl bromides and chlorides and C–H activation of methane [11]. Our group have developed a facile procedure for the synthesis of heteroaryl coordinated chelating NHC palladium complexes featuring different N-substituents, chelating rings or NHC backbones (Fig. 1. **Ia–f**) [10a,10b]. The preliminary research proved their efficient catalytic activity towards the 2-arylation of (benzo)oxazoles or Suzuki cross-coupling in water [10a,10b]. To investigate the catalytic activity further and establish the relationship between the structure and the activity, complexes **Ig–h** were synthesized and structurally characterized.

Coumarins has been widely used in the synthesis of

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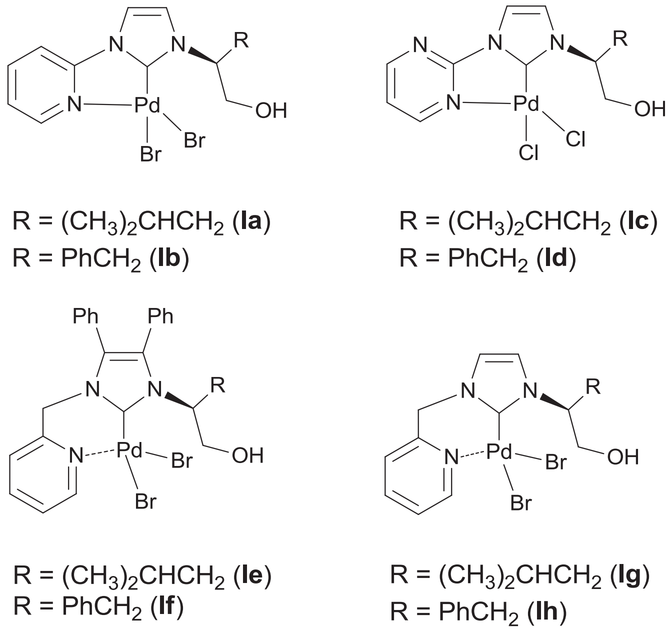


Fig. 1. Chelating NHC palladium complexes used here.

pharmaceutically active compounds [12], and several 3-phosphorated coumarins have been proved to exhibit cytotoxicity on some human leukemia cell lines as well as high alkylating activity [13]. Selective synthesis of phosphorated coumarins has been a quite active topic and significant progress has been achieved through transition-metal-catalysed C—P bond construction [14]. Despite the great success achieved in NHC palladium catalysed cross-coupling reactions [8] and the transition-metal-catalysed C—P bond construction [15], to the best of our knowledge, direct C—H phosphorylation remains an enormous challenge and the NHC palladium catalysed C—P bond formation has not been reported. Here we present the catalytic activity of a series of heteroaryl coordinated chelating NHC palladium complexes towards the selective phosphorylation of coumarins.

2. Results and discussion

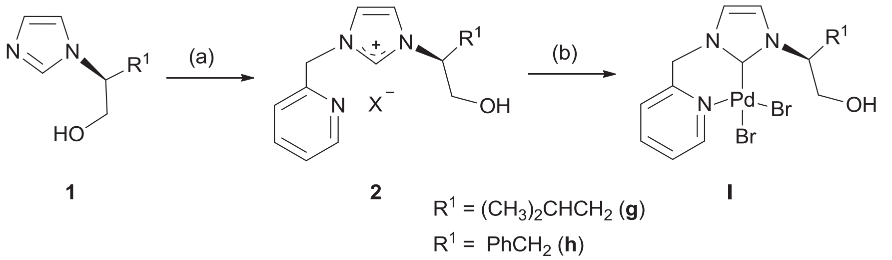
2.1. Synthesis of the chelating NHC palladium complexes

Following literature reports, chiral imidazole alcohols **1** were obtained conveniently from *L*-amino alcohol [10a,10b]. The reaction of the imidazole alcohols **1** with 2-bromomethyl-pyridine in refluxing CH_3CN produced the picolyl hydroxyalkyl di-substituted imidazolium salts **2g**—**h** (Scheme 1), which were purified by column chromatography and characterized by NMR and MS technologies. In the NMR spectra, the significantly downfielded shift of the NC*H*N protons (9.41 and 9.49 ppm in **2g**—**h**, 7.48 and 7.65 ppm in alcohol **1a**—**b**) and the additional signals appeared in the aromatic region indicated the formation of imidazolium salts [10a,10b]. The signals of NC*H*N protons in picolyl substituted imidazolium salts **2g**—**h** (9.41 and 9.49 ppm) showed an obvious upfielded shift compared to those in 2-pyridinyl substituted imidazolium bromides **2a**—**b** (10.25 and 10.17 ppm) and 4,5-diphenyl-substituted analogues **2e**—**f** (9.93 and 10.31 ppm). The difference between **2g**—**h** and **2a**—**b** maybe explained that the insertion of methylene group interrupted the conjugate system formed between pyridinyl and imidazolium ring. The difference between **2g**—**h** and **2e**—**f** maybe contributed to the anisotropy of the 4,5-diphenyl substituents. The formation of the imidazolium salts was further confirmed by the appearance of $[M—Br]^+$ signals in MS analysis. Direct metalation of the imidazolium salt with $PdCl_2$ in the presence of NaOAc and NaBr in heating CH_3CN produced the six-membered chelating NHC palladium complexes **Ig**—**h** in moderate yields (Scheme 1). The formation of the chelating NHC palladium complexes was observed from ^1H NMR, which showed conspicuous absence of the NC*H*N resonances of the reacting imidazolium bromides **2g**—**h**. The molecular structure of **Ih** was further characterized unambiguously by the single-crystal X-ray diffraction studies.

Fig. 2 shows the molecular structure of **Ih** with selected bond lengths and bond angles listed in the caption. As shown in Fig. 2, the palladium atom adopts a slightly distorted square-planar coordination constituted by carbene, pyridine nitrogen donor and two bromides, with the six-membered chelating ring adopts a boat conformation. Similar to complexes **Ia**-**f**, the hydroxyl group hangs freely [10a,10b]. The $Pd—C_{carbene}$ bond distances of 1.980(8) Å is slightly shorter than those of the 2-pyridinyl coordinated five-membered chelating analogue **Ia** (1.990(14) Å) and the 4,5-diphenyl-substituted six-membered chelating analogue **2f** (1.997(9) Å) [10a,10b]. The Pd—N distance (2.054(6) Å) and Pd—Br distances (2.4911(10) Å and 2.4247(10) Å), are very similar to those of **Ia** (2.061(10) Å, 2.4726(12) and 2.4148(15) Å) and **If** (2.071(5) Å, 2.4918(8) Å and 2.4162(9) Å), with the Pd—Br bond *trans* to the $Pd—C_{carbene}$ bond slightly longer than those *trans* to the Pd—N bond [10a,10b].

2.2. Catalytic studies

The substitution pattern on the backbone or nitrogen atom has large effect on the electronic and steric properties, and coordination mode of the NHCs, hence leading to the formation of different catalytic active species. Using the reaction of coumarin with dimethyl phosphite as a model reaction, the catalytic activity of complexes **Ia**—**h** towards the phosphorylation of coumarins was studied and the 3-phosphorated coumarin was obtained selectively (Table 1). The results in Table 1 showed that the chelating complexes **Ia**—**h** all showed moderate catalytic efficiency for the model



Scheme 1. Synthesis of the imidazolium salts and chelating NHC palladium complexes. (a) 2-bromomethyl-pyridine, CH_3CN, 85 °C, 36 h; (b) $PdCl_2$, NaOAc, NaBr, CH_3CN, 80 °C, 10 h, N_2.